30 April 2018
EMA/CVMP/ERA/609438/2017
Committee for Medicinal Products for Veterinary Use (CVMP)

# Overview of comments received on 'Guideline on assessing the toxicological risk to human health and groundwater communities from veterinary pharmaceuticals in groundwater' (EMA/CVMP/ERA/103555/2015)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

| Stakeholder no. | Name of organisation or individual |
|---|---|
| 1 | European Group for Generic Veterinary Products (EGGVP) |
| 2 | Friends of the Earth Germany (BUND) |
| 3 | German Limnological Society |
| 4 | International Federation for Animal Health Europe (IFAH-Europe) |
| 5 | Institute of the Republic of Slovenia for Nature Conservation |
| 6 | Institut für Grundwasserökologie (IGÖ) |
| 7 | Karst Research Institute - Scientific Research Centre of the Slovenian Academy of Sciences and Arts |
| 8 | Institute of Groundwater Ecology (DE) |

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| Stakeholder no. | Name of organisation or individual |
|---|---|
| 9 | Pesticide Action Network - Pestizid Aktions-Netzwerk e.V. (PAN Germany) |
| 10 | Public Service Agency, Slovenia |
| 11 | The Dutch National Institute for Public Health and the Environment (RIVM) |
| 12 | Society for Cave Biology, Tular Cave Laboratory |
| 13 | Società Adriatica di Speleologia, Italy |
| 14 | Institute of Ecosystem Study of the CNR – National Council Research of Italy |
| 15 | German Environment Agency (UBA) |
| 16 | University of Roehampton, UK |
| 17 | Bundeskontaktstelle Wasser |
| 18 | European Environmental Bureau (EEB) |

# 1. General comments – overview

| | Stakeholder no. | General comment | Outcome |
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| 1 | 2 | The draft is an important first and timely step into the right direction. VMP were missing so far although, as stated in the draft, compounds are chemically very similar to pesticides (biocides) and pharmaceuticals for humans.<br><br>Pharmaceuticals do not appear and react as "single" substances in the aquatic environment and its ecosystems. Thus, mixture effects of different combinations of such chemicals have to be considered. Furthermore, aquifers may be affected by several stressors, above all nitrate, pesticide and/or thermal pollution. Hence, it is recommended to establish a realistic scenario for assessing the effects of pharmaceuticals in groundwater ecosystems and to establish relevant requirements in the framework of the approval of | Thank you for your comment.<br><br>Not accepted. The guideline has been prepared in line with the regulatory framework for VMPs, and this is related to the authorization of single active ingredients. |

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| | | active substances and products of veterinary pharmaceuticals.<br><br>From an ecological perspective, there is no safe concentration, but there is only a predicted no effect concentration or a concentration where no effect could be measured with the tests/studies applied.<br><br>The additional assessment factor of 10 is a first approach and may be suitable for a period of transition. However, the actual toxicity of veterinary pharmaceuticals to groundwater communities and ecosystems needs urgently to be tested with appropriate test systems and protocols (chronic tests) for groundwater – and this should be the case also for all other pollutants already listed in the WFD and GWD. Special attention should be given to antiparasitic.<br><br>In order to confirm the precautionary principle and to prevent the deterioration of less contaminated groundwater bodies, we explicitly reject introducing a risk assessment for any certain pharmaceutical substance having regard to a pollution scenario above 0.1 µg/l (for example, cf. lines 37-38 or 100-101) unless there are validated test methods using typical groundwater organisms in environmentally realistic conditions. Even if current findings of eco-toxicological assessments suggest no unacceptable risk for a relevant ecosystem at such predicted higher pollution (levels) one has to consider that relevant tests still go along with several unsolved methodological shortcomings which question the “ecological validity” of respective tests (eg. choice of organisms & test period). Apart of this, the effectiveness of specific risk | Accepted. Where “safe concentration” was mentioned in the text, this has been changed according to the proposed suggestion. See in pages 3, 4, 6 and 8.<br>Noted. The additional assessment factor of 10 is used to address the added uncertainty of lack of knowledge on the sensitivity of groundwater species and ecosystems. At the time being, there are no standardized test protocols to evaluate the effects of chemicals towards GW species. The ERAWP agrees that an effort in this direction is needed to address the knowledge gap. In addition, this AF will be helpful in managing risk of parasiticides.<br><br>Noted. While not explicitly covered in this guideline, the current veterinary legislation takes into consideration that any environmental risk identified during a marketing authorisation procedure has to be factored in the benefit risk balance of the product, bearing in mind that an environmental impact resulting from the use of a VMP can lead to the refusal to authorise a product. |

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| | | reduction measures is usually not proven under realistic worst case scenarios. As a consequence risks might be overlooked. And what is even more serious: To accept a pollution (level) above 0.1 µg/l would contradict current approval standards and provisions for drinking water and groundwater protection according to Article 4.1 WFD (Water Framework Directive). Although the draft guideline includes provisions in order to comply with standards for relevant substances which are simultaneously used as biocides & pesticides ( = application of GQS of Annex I GWD) or covered according to Annex VIII WFD, open questions for implementation remain. It is obvious that further clarification is necessary which bind resources and an effective protection of environment and human health. Hence, we urge to ensure the requirement that:<br><br>• any pharmaceutical should only get approval when its concentration (level) is predicted not to exceed 0.1 µg/l in the groundwater, unless<br>• an appropriate risk assessment demonstrates for a relevant substance, that stricter EQS/GQS or threshold value is necessary in order to protect groundwater and/or human health.<br><br>Furthermore, the protection of groundwater should be effectively considered and prioritized when assessing the risks and benefits of a certain veterinary pharmaceutical. This is not guaranteed with the suggested procedure. | |

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| | | There are some general aspects to be considered:<br>- All data used for the approval procedure have to be available for the public. At present, they cannot be used for the deduction of EQS due to intellectual property rights.<br>- No approval for persistent or non-degradable veterinary pharmaceuticals<br>- Veterinary pharmaceuticals, which accumulate in the groundwater or occur in surface waters used for drinking water purposes in concentrations > 0,1 µg/l have to be withdrawn from circulation<br>- When assessing pharmaceuticals in the framework of the approval procedure it is necessary to compare such substances with alternatives which are demonstrated to be more environmental friendly. Such sound options should get priority. | Noted. Considerations on the access to data used in marketing authorisations are outside the scope of this guideline.<br><br>Regarding provisions for VMPs with specific physicochemical properties, both the environmental and human health risk assessment proposed in the guideline already consider such. For the environment, the calculations of predicted environmental concentration take into account persistence of substances, and for human health assessments pharmacological, toxicological and microbiological data are used to ensure its safety. Additionally, the concept of 'comparative assessment' is noted but it is outside the scope of this guideline. |
| 2 | 3 | The draft is an important first and timely step into the right direction. VMP were missing so far although, as stated in the draft, compounds are chemically very similar to pesticides (biocides) and pharmaceuticals for humans.<br><br>Pharmaceuticals do not appear and react as "single" substances in the aquatic environment and its ecosystems. Thus, mixture effects of different combinations of such chemicals have to be considered. Furthermore, aquifers may be effected by several stressors, above all nitrate, pesticide and/or thermal pollution. Hence, it is recommended to | Thank you for your comment.<br>Please refer to the answer to comment 1, above which already addresses the first part of your comment. |

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| | | establish a realistic scenario for assessing the effects of pharmaceuticals in groundwater ecosystems and to establish relevant requirements in the framework of the approval of active substances and veterinary products.<br><br>From an ecological perspective, there is no safe concentration, but there is only a predicted no effect concentration or a concentration where no effect could be measured with the tests/studies applied.<br><br>The assessment factor of 10 is a first approach and may be suitable for a period of transition. However, the actual toxicity of veterinary pharmaceuticals to groundwater communities and ecosystems needs urgently to be tested with appropriate test systems and protocols (chronic tests) for groundwater – and this should be the case also for all other pollutants already listed in the WFD and GWD. Special attention should be given to antiparasitica.<br><br>There are some general aspects to be considered:<br>- All data used for the approval procedure have to be available for the public. At present, they cannot be used for the deduction of UQN due to intellectual property rights.<br>- No approval for persistens or nondegradable veterinary pharmaceuticals<br>- Veterinary pharmaceuticals, which accumualate in the groundwater or occur in surface waters used for | |

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| | | drinking water purposes in concentrations > 0,1 µg/l have to be withdrawn from circulation | |
| | | In chapter 4.2, references should be provided for all predictions made on the differences between surface and groundwater taxa. | Noted. References were already added in the previous draft, and an additional reference has now been included (Kolar & Finizio, 2017). |
| | | A table of abbreviations might be helpful. | Accepted. A glossary section has been added to the document. |
| | | Keep a consistency in the wordings “gw” or “groundwater” as well as plain or subscript “PECgroundwater” or “$PEC_{groundwater}$”. | Accepted. |
| | 4 | IFAH-Europe welcomes the opportunity to comment on this draft guideline.<br>This proposed GL goes beyond the scope of the concept paper EMA/CVMP/ERA/718229/2012:<br>“*The Committee recommends the development of a guideline outlining the methodology to perform a risk assessment for both human health and the environment in cases where the concentration of residues of veterinary medicinal products in groundwater is estimated to be above the trigger value of 0.1 µg/l.*”<br>This guideline now also includes cases with $PEC_{groundwater}$ below 0.1 µg/L. Is a significant change to the scope like this possible without an additional concept paper? | Thank you for your comment.<br>A concept paper was published for consultation prior to the development of this guideline. The purpose of the concept paper is to identify issues that might need to be further reflected or addressed during the development of the guideline. During the consultation of the concept paper on the toxicological risk of VMPs in groundwater a number of comments with regards to the trigger value of 0.1 µg/l were provided by several stakeholders, and such were considered by experts during the drafting of this guideline. Additionally, as comments to the draft guideline are considered during the preparation of the final guidance, the CVMP considered that an additional consultation of a new concept paper was not needed. |

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| 3 | 4 | We welcome the possibility to perform a risk assessment when the GQS value is overpassed, instead of just the hazard identification. | Thank you for your comment. |
| 4 | 4 | Inserting a glossary of the acronyms used would be very helpful (i.e. PNEC, EQS, ERA, PEC, GQS, VMP, MTC, ADI, BW, P, Cw, DT50, Koc, RQgw) | Thank you for your comment. A glossary section has been added to the document. |
| 5 | 5 | Slovenia has some of the greatest subterranean biodiversity in the whole world, especially the aquatic fauna with 200 species is by far the richest. The state in subterranean habitats has been observed to deteriorate due to underground water pollution on more locations. We are especially worried, because the olm (*Proteus anguinus*), the showpiece species of nature protection in Slovenia, is endangered. The assessment of the status of the species carried out in 2007 and 2013 as a part of reporting under Habitat Directive related it as inadequate (U1).<br><br>We express:<br>- Support on the approach of the Guideline, in which the groundwater is not considered only as a source of drinking water, but also as a unique ecosystem; support on the approach by which the subterranean ecosystems are one of the objectives of the environmental protection.<br>- Support on the proposed Guideline, by which the ecotoxicological data should also be taken into account when determining safe concentrations for groundwater, in particular when substances are highly toxic to the aquatic environment.<br><br>We propose a similar approach in which safer concentration of | Thank you for your comment.<br><br>Noted. |

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| | | nitrates, pesticides, biocides and animal food additives will be determined for groundwater dependent ecosystems, as an integral part of the environmental protection in EU. | Noted. However, the assessment of these substances falls within the responsibility of other legislations and are therefore outside the scope of this guideline. |
| 6 | 6 | The draft is an important first and timely step into the right direction. VMP were missing so far although, as stated in the draft, compounds are chemically very similar to pesticides (biocides) and pharmaceuticals for humans.<br><br>Pharmaceuticals do not appear and react as "single" substances in the aquatic environment and its ecosystems. Thus, mixture effects of different combinations of such chemicals have to be considered. Furthermore, aquifers may be affected by several stressors, above all nitrate, pesticide and/or thermal pollution. Hence, it is recommended to establish a realistic scenario for assessing the effects of pharmaceuticals in groundwater ecosystems and to establish relevant requirements in the framework of the approval of active substances and products of veterinary pharmaceuticals.<br><br>From an ecological perspective, there is no safe concentration, but there is only a predicted no effect concentration or a concentration where no effect could be measured with the tests/studies applied.<br><br>The additional assessment factor of 10 is a first approach and may be suitable for a period of transition. However, the actual toxicity of veterinary pharmaceuticals to groundwater communities and ecosystems needs urgently to be tested with appropriate test systems and protocols (chronic tests) for | Thank you for your comment. Please refer to the answer to comment 1 and 2, above. |

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| | | groundwater – and this should be the case also for all other pollutants already listed in the WFD and GWD. Special attention should be given to antiparasitics.<br><br>In order to confirm the precautionary principle and to prevent the deterioration of less contaminated groundwater bodies, we explicitly reject introducing a risk assessment for any certain pharmaceutical substance having regard to a pollution scenario above 0.1 µg/l (for example, cf. lines 37-38 or 100-101) unless there are validated test methods using typical groundwater organisms in environmentally realistic conditions.. Even if current findings of eco-toxicological assessments suggest no unacceptable risk for a relevant ecosystem at such predicted higher pollution (levels) one has to consider that relevant tests still go along with several unsolved methodological shortcomings which question the "ecological validity" of respective tests (eg. choice of organisms & test period). Apart of this, the effectiveness of specific risk reduction measures is usually not proven under realistic worst case scenarios. As a consequence risks might be overlooked. And what is even more serious: To accept a pollution (level) above 0.1 µg/l would contradict current approval standards and provisions for drinking water and groundwater protection according to Article 4.1 WFD (Water Framework Directive). Although the draft guideline includes provisions in order to comply with standards for relevant substances which are simultaneously used as biocides & pesticides ( = application of GQS of Annex I GWD) or covered according to Annex VIII WFD, open questions for implementation remain. It is obvious that further clarification is necessary which bind resources and an effective protection of environment and human health. Hence, we urge to ensure | |

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| | | the requirement that:<br><br>• any pharmaceutical should only get approval when its concentration (level) is predicted not to exceed 0.1 µg/l in the groundwater, unless<br>• an appropriate risk assessment demonstrates for a relevant substance, that stricter EQS/GQS or threshold value is necessary in order to protect groundwater and/or human health.<br><br>Furthermore, the protection of groundwater should be effectively considered and prioritized when assessing the risks and benefits of a certain veterinary pharmaceutical. This is not guaranteed with the suggested procedure.<br><br>There are some general aspects to be considered:<br>- All data used for the approval procedure have to be available for the public. At present, they cannot be used for the deduction of EQS due to intellectual property rights.<br>- No approval for persistent or non-degradable veterinary pharmaceuticals<br>- Veterinary pharmaceuticals, which accumulate in the groundwater or occur in surface waters used for drinking water purposes in concentrations > 0,1 µg/l have to be withdrawn from circulation<br>- When assessing pharmaceuticals in the framework of the approval procedure it is necessary to compare such substances with alternatives which are demonstrated to be more environmental friendly. Such sound options should get priority. | |

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| 7 | 7 | Groundwater ecosystems constitute the largest terrestrial freshwater biome with 95% of global liquid freshwater stored. Comprising 15% of the earth's surface, karst represents 30% of the land area of Europe. There is an urgent need to integrate evolutionary and ecological research for developing a holistic perspective of the function roles of biodiversity and ecosystem services and predicting global changes under alternative groundwater resource use scenarios. | Thank you for your comment. |
| 8 | 8 | The draft is an important first and timely step into the right direction. VMPs were missing so far although, as stated in the draft, compounds are chemically very similar to pesticides (biocides) and pharmaceuticals for humans.<br><br>From an ecological perspective, there is no 'safe' concentration, there is only a predicted no effect concentration or a concentration where no effect could be measured with the tests/studies applied. Maybe the statement of a 'safe' concentration can be avoided.<br><br>The additional assessment factor of 10 is a first approach and may be suitable for a period of transition. However, the actual toxicity of veterinary pharmaceuticals to groundwater communities and ecosystems needs urgently to be tested with appropriate test systems and protocols (incl. chronic tests) for groundwater – and this should be the case also for all other pollutants already listed in the WFD and GWD. | Thank you for your comment. Please refer to the answer to comment 1 above. |
| 9 | 9 | In intensive husbandry large quantities of veterinary pharmaceuticals are used. A considerable part of them ends up in the environment and leads to contamination of different environmental compartments and their organisms including | Thank you for your comment. The point regarding the Groundwater Directive and the lack of GQS for veterinary medicines is noted. However, establishing quality standards for veterinary |

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| | | groundwater. Up to present groundwater quality standards (GQS), as defined by the groundwater directive (GWD) for pesticides and biocides, have not been established for veterinary pharmaceuticals although some active substances are identical and the groundwater should be protected from all contaminations of active ingredients irrespective of their use types or risks. In PAN Germany's view it is about time that the GWD is revised in order to fill this gap and include all pharmaceuticals in Annex I. | medicines and the implications for this for the groundwater directive, fall outside the mandate of the CVMP and are outside the scope of this guideline. |
| | | Groundwater as a valuable and vulnerable natural resource, as an ecosystem, as the largest body of freshwater in the European Union, and as a main source of public drinking water supply is of inestimable value for current and future generations and must be protected from deterioration and chemical pollution of any kind of contaminants, especially because vulnerability of groundwater communities is still unclear and disturbances might be irreversible. This tremendous value can hardly be offset against the benefit of a single veterinary medical product especially as the authorization of veterinary medical products does not oblige to carry out a comparative assessment and/or prove the medical necessity for the placing on the market of a specific VMP before the risk-benefit assessment. | Noted. |
| | | PAN Germany welcomes the initiative to provide an improved methodology for performing a risk assessment of groundwater contamination by veterinary medicinal products for PEC < 0.1 | Noted. |

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| | | µg/l. We especially welcome that the protection of groundwater is not only conducted to secure groundwater as a source of human drinking water but also as a vulnerable ecosystem with its own intrinsic value.<br><br>Groundwater communities do not only have to cope with the occurrence of a single veterinary substance but with the occurrence of mixtures of different substances. Especially when it comes to antimicrobials this is very relevant: antimicrobials are used in large quantities in intensive husbandry, antimicrobial substances have already been detected in groundwater bodies, and investigations of shallow groundwater aquifers in northern Germany have revealed that the detected antimicrobial substances - like sulfadimidine, sulfamethoxazole and sulfadiazine, belong to the same group of substances (see UBA, 2016: Aufklärung der Ursachen von Tierarzneimittelfunden im Grundwasser – Untersuchung eintragsgefährdeter Standorte in Norddeutschland. http://www.umweltbundesamt.de/publikationen/antibiotika-antiparasitika-im-grundwasser-unter).<br>Before this background we are very concerned that cumulative or synergistic effects of mixtures of VMPs are not addresses in the draft guideline on risk assessment. Different VMPs are applied and groundwater communities can be affected by different VMPs at the same time.<br>This scenario is not taking into account in the proposed risk assessment procedure for VMPs / active ingredients with PEC < 0.1 µg/l though examples for considering synergistic effects | Noted. Regarding the comment on mixtures, please refer to the answer to comment 1 above. In addition, in the pesticide regulation a risk assessment for mixtures of pesticides is performed only when commercial formulations are considered (inclusion in ANNEX III). When that is the case, the concentration addition model (CA model) is used as a worst case and toxicological endpoints should be provided on commercial products rather than active ingredients |

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| | | of mixtures are provided by other spheres of regulation - e.g. on pesticides and biocides. For example, according to the Pesticide Regulation 1107/2009 the risk assessment of pesticides has to take into account known cumulative and synergistic effects. PAN Germany recommends the amendment of an equal phrase in the present draft.<br><br>The GWD also defines a groundwater quality standard (GQS) of 0.5 µg/l (total limit value) for mixture exposure of groundwater by pesticides, including active substances, their relevant metabolites, degradation products and reaction products. This sum parameter should also apply accordingly to pharmaceutical contaminants in groundwater. In addition, other contaminations like pesticides or nitrate appear in the aquatic environment and react within its ecosystem. Provisions are needed to take this into account when calculating the risk to human health and groundwater communities from veterinary pharmaceuticals in groundwater.<br><br>The aim of groundwater protection was always to keep groundwater free of contamination. The existing groundwater quality standards (GQS) of 0.1 µg/l (based on the drinking water limit) for single substances had been established in a time where 0.1 µg/l was the usual limit of detection and predicted concentrations below 0.1 µg/l were interpreted as equivalent to 'no emission into groundwater'. With improved detection technology and before the background of improved knowledge about substances, organisms and their interaction, | Noted. Indeed, environmental quality standards for the groundwater (GW EQS) are set to provide criteria which should be meet in the monitoring of chemical quality of groundwater. However, the EQS of 0.5 µg/L for mixtures in groundwater is currently in place for the framework of risk assessment on pesticides and biocides. At this time, the environmental risk assessment of VMPs in groundwater is assessed against the threshold value of 0.1 µg/.<br><br>Noted. |

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| | | the former detection limit of 0.1 µg/l can no longer be regarded as a safe limit value if the PNEC is below 0.1 µg/l. PAN Germany welcomes that the draft does recognize that, and takes into account that a concentration below 0.1 µg/l does not always mean that there is no risk.<br><br>On the other hand we are very concerned that the draft calls for lowering the protection standards for human health and the ecosystem by accepting contaminations above 0.1 µg/l if the risk assessment of the single substance according to the current state of science shows no risk. This concept contradicts the precautionary principle that the contamination of groundwater by active ingredients is not acceptable and it totally ignores the risks of mixtures.<br><br>PAN Germany welcomes the implementation of an additional assessment factor of 10 for better securing groundwater ecosystems. This approach should be accompanied by further research on acute and chronic toxicity of veterinary pharmaceuticals to groundwater organisms/communities and groundwater ecosystems and by establishing specific test systems for groundwater. Special attention should be paid to antibiotics (as antimicrobial resistance is an emerging issue and as antibiotics account for the majority of used VMPs (in tons) and for antiparasitics (due to their specific damaging effect on organisms).<br><br>The effort to enhance groundwater protection from the | Not accepted.<br>The guideline has been drafted to move towards an environmental risk assessment based on a risk ratio approach (PEC/PNEC) for single active ingredients.<br><br>Noted. Please see the answer to comment 1 above. |

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| | | adverse effects of VMPs as laid down in the draft should be accompanied by the following measures:<br>• Promotion of animal health and welfare in animal husbandry to increase animal well-being and consequently reduce the need and use for VMPs.<br>• Authorisation of VMPS should establish<br>- specific procedures for phasing-out and substituting environmentally-hazardous products and<br>• Authorisation should be denied<br>- if environmentally sustainable alternatives (products/processes) exist, and<br>- for substances that are regarded as especially hazardous to the environment such as PBT substances (persistent, bio-accumulative, and toxic) and vPvB substances (very persistent and very bio-accumulative). | Noted. Please see the answer to comment 1 above. |
| 10 | 10 | - It is of outmost importance that the underground ecosystems are one of the aims of environmental protection.<br>- It is of outmost importance that underground water are not concerned only as source of drinking water, but also as an important ecosystem.<br>- It is necessary to take into consideration also toxicological data in assessing the safe concentrations for underground waters, especially when substances of high toxicity are | Thank you for your comment. |

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| | | concerned.<br>- We suggest similar approaches are used in establishing safe concentration of nitrate, pesticides, biocides and food additives for animals, where protections of underground ecosystems must be considered as one of the most importan goals in environmental protection. | Noted. However, the assessment of these substances falls within the responsibility of other legislations and are therefore outside the scope of this guideline. |
| 11 | 11 | Reference is made to Directive 2006/118/EC, Annex I, using the limit value of 0.1 µg/L for 'pesticides and biocides'. However, the use of this reference is incomplete as the reference refers to 'Active substances in pesticides, including their relevant metabolites, degradation and reaction products'. The inclusion of metabolites, degradation products and reaction products is highly relevant for VMPs as these can be generated at three potential stages (in the target animal, during manure storage and in soil). Since metabolites or transformation products are generally more mobile in soils and may also be more toxic and more persistent than their parent substance [examples are fenbendazol and thiabendazol], addressing their potential occurrence in groundwater is of high relevance. This is an established part of the risk assessment of plant protection products and biocides, is included in the groundwater Directive (2006/118/EC) and the drinking water Directive (98/83/EC as amended) and should be incorporated in the VMP risk assessment strategy for groundwater as well.<br><br>The risk assessment for metabolites could be performed similar to the risk assessment methodology for PPP's and | Accepted. |

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| | | biocides.<br><br>The reference list is incomplete and inconsistent. E.g. FOCUS (2000) and (EMA 2005) are missing, etc.<br><br>The authors cite ' CVMP TGD (2016)', but this reference is not in the list. It is included in the list as European Medicines Agency (EMA). 2016. Please correct and make citing consistent.<br><br>In describing the characteristics of groundwater ecosystems with respect to sensitivity and resilience in sections 4.2, 4.2.2, 4.2.3 the text consequently uses the word 'species'. Although 'species' does comprise micro-organisms in a literal sense, the text is not explicit in that for many subsurface systems, the biomass largely consists of micro-organisms. Protection of 'groundwater' and especially its self-purifying properties, also includes protection of microbial subsurface communities in those types of environment. This deserves attention and could be done by adding a few words. A text proposal is given in the section with specific comments.<br><br>Groundwater is currently the only exposure route of humans to VMPs via the environment. Exposure via food from crops grown on fields fertilised with VMP containing manure or irrigated with VMP containing water is currently not assessed. Could this be an omission? | Accepted.<br><br>Accepted.<br><br>Accepted. A sentence has been added to clarify the term ‘species’.<br><br>Not accepted. The plant VMP uptake from amended soil or from irrigated soil with VPM containing water is out of the scope of this guideline. |

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| | | The EU Drinking water directive (98/83/EC) is just as relevant as the groundwater directive (2006/118/EC), since groundwater is a source for drinking water. Reference to the drinking water directive should be made, where appropriate. | Accepted. A reference has been added in the introduction section |
| | | The CVMP approach for the risk assessment of groundwater up to now (' concentrations above 0.1 µg/L have been considered unacceptable for all substances'), as mentioned in line 56-57, is in line with EU legislation on groundwater and drinking water, as regards pesticides, biocides , and their relevant metabolites, degradation products and reaction products.<br>In Chapter 4, CVMP outlines extensively that groundwater both as an environmental compartment and as an ecosystem is very vulnerable to pollution by xenobiotic substances, has low capacity to cope with disturbances and that it may require decades to recover, if at all. This again expresses their concerns with respect to pollution of groundwater bodies.<br>In the current document, a switch is made from an assessment procedure based on the precautionary principle to a risk based procedure without any rationale. CVMP is moving away from assessment procedures for plant protection products and biocides, which sometimes contain the same active substances.The rationale for this switch should be better explained or may have to be re-discussed.<br>Currently, the approach taken in the Netherlands for anthropogenic substances in sources for drinking water (other than pesticides and biocides), is that a 0.1 µg/L signaling | Noted. The rational for the risk assessment presented for human health and for the environment is developed based on a risk assessment based on reliable laboratory data, moving away from a precautionary principle when a robust risk assessment methodology could be used to characterise such risks. |

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| | | value should not be exceeded [Ministry of Infrastructure and the Environment, 2015, Dutch protocol on monitoring and assessment of drinking water sources under the WFD]. This is a precautionary value which allows the production of drinking water with only natural purification processes. This is in line with the strategy set out in the WFD which is based on prevention and sustainability. When this value is exceeded a risk assessment is performed. When a risk is identified, this increases the need for risk management options. RIVM suggests to consider a similar approach: if a substance exceeds the signaling value, this could already be part of the benefit/risk assessment and risk mitigation measures could be applied, from a precautionary principle. If, in addition to this, a risk is identified, this could then further increase the weight of the risk in the benefit/risk evaluation.<br><br>CVMP states in line 107-111, that substances which are also marketed as a plant protection product (PPP) or biocide, should not enter groundwater in concentrations ≥ 0.1 µg/L. It is unclear how this should be read for substances which used to be marketed as PPP or biocide but not anymore. Furthermore, we foresee that this will cause a lack of level playing field between applicants, since some will have to adhere to the 0.1 µg/L limit and others, which are currently not marketed as PPP or biocide but which may have a similar mode of action, do not have to adhere to this limit. It should be acknowledged that the mentioning of PPPs and biocides in the groundwater and drinking water legislation, is based on | Noted. However, the risk assessment presented has been developed in line with the framework for the risk assessment for VMPs for which provisions on limit values are not mentioned in the legislation. Thus, the assessment of the built on methodology using scientific data. |

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| | | their biological mode of action, which is essence is not different for VMPs. Thus it seems undesirable to make a difference between PPPs/biocides and VMPs, or to make a difference between VMPs that are also PPPs/biocides and other VMPs. | |
| 12 | 12 | - We support the approach of the Guideline, in which the groundwater is not considered only as a source of drinking water, but also as a unique ecosystem. We also support the approach by which the subterranean ecosystems are one of the objectives of the environmental protection.<br><br>- We support the proposed Guideline, by which the ecotoxicological data should also be taken into account when determining safe concentrations for groundwater, in particular when substances are highly toxic to the aquatic environment.<br><br>- We propose a similar approach in which safer concentration | Thank you for your comment. Please refer to the answer to comment 10, above. |

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| | | of nitrates, pesticides, biocides and animal food additives will be determined for groundwater dependent ecosystems, as an integral part of the environmental protection in EU. | |
| 13 | 13 | We feel it is very important and we support the approach of the guidelines in which the underground water is considered in its complexity: like an unique ecosystem and not only like a source of drinking water.<br>We also support the approach by which underground ecosystems are one of the goals of environmental protection. Only bearing in mind this aspect and the integrity of the delicate balance in hypogeal life we will have resources for a future where water will be more and more precious.<br><br>We support the proposed Guideline, by which the ecotoxicological data should also be taken into account when determining safe concentrations for groundwater, in particular when substances are highly toxic to the aquatic environment.<br><br>The groundwater ecosystem is considered more vulnerable than many other aquatic ecosystems. Therefore we support the approach of the guidelines for a risk assessment that considers the concentration of toxic elements in concentrations below 0.1 micrograms per liter.<br><br>We also believe it is important to support all forms of research, knowledge dissemination and education of new generations about the uniqueness of underground ecosystems, and the most appropriate strategies for their conservation and protection and for the best balance between | Thank you for your comment. |

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| | | human activities and the environment. | |
| 14 | 15 | We welcome the draft guideline on the assessment of the toxicological risk to humans and the environment of veterinary pharmaceuticals in interstitial and hypogean groundwater communities.<br>The draft is engaged in main aspects of European risk assessment strategies.<br><br>We appreciate the general chapter on the groundwater quality standard (0.1 µg/l) and the European principles of precautionary. However, the consequences arising from the assessment approaches provided in the guideline draft are not in line with the precautionary principle.<br><br>It seems not to be based on logical reasons to avoid a risk based assessment for human health if the predicted concentration is below 0.1 µg/l, especially for highly active substances as pharmaceuticals – e.g. hormones, parasiticides.<br><br>Furthermore we are missing the consideration of metabolites/transformation products in the environmental and health risk assessment approaches.<br><br>In general, the wording “safe” in the context of predicted no effect concentrations (PNEC) or environmental concentrations should be avoided as this does not comply to the regulatory approaches of uncertainty and ecological principles. The | Thank you for your comment.<br><br>Noted. The guideline has been drafted to move towards an environmental risk assessment based on a risk ratio approach (PEC/PNEC).<br><br>In line with the concept paper, the scope of the assessment for human health is limited to those cases where $PEC_{groundwater}$ is equal to or above the GQS of 0.1 µg/l.<br><br>Noted. Please see answer to comment 11 above<br><br>Accepted. See answer to comment 1 above. |

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| | | wording “safe” implies a degree of guaranty for species or ecosystem communities which is not deducible from environmental risk assessment.<br><br>Furthermore, it might be appropriate to add a list of abbreviations to improve the legibility of the guideline. | Accepted. |
| 15 | 16 | Thank you for the opportunity to comment on the draft guidelines on assessing the toxicological risk to human health and groundwater communities from veterinary pharmaceuticals in groundwater. I am delighted that the draft recognises the unique nature of groundwater ecosystems and their vulnerability resulting from their prolonged exposure to chemicals, their sensitivity to chemical stressors and their low resilience to perturbations.<br><br>The current guidelines do not include ecotoxicity testing for the determination of the safe concentration of a substance in water with species other than surface water species. As a result the draft guidelines suggest an additional assessment factor of 10 should be applied to extrapolate the PNEC (groundwater) from the PNEC (surface water) to allow for groundwater ecosystem vulnerability. Although this is a very useful first step it is a very blunt instrument indeed. As there is very limited data indeed on groundwater organism ecotoxicological responses the proposed assessment factor of 10 may be too high or too low. Further work to determine the responses of groundwater model organisms to chemical stressors including veterinary pharaceuticals should be a | Thank you for your comment.<br><br>Noted. We acknowledge that a risk assessment with model groundwater species would be important to characterise the risk of VMPs and other stressors in groundwater systems. However, at this point in time there are no internationally agreed guidelines to address the acute or chronic effects of chemical stressors to groundwater organisms. |

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| | | priority to allow the refinement of risk assessment procedures for groundwater ecosystems. | |
| 16 | 17 | 2012 wurden in Deutschland rund 1.619 Tonnen Antibiotika an Tierärzte abgegeben, was etwa dem Zwei- bis Dreifachen des Antibiotikaeinsatzes in der Humanmedizin entspricht. Je nach Wirkstoff werden etwa 60 bis 80 Prozent der verabreichten Menge unverändert mit dem Kot und Urin der Tiere ausgeschieden; mit der Gülle gelangen sie dann auf die Böden. Bisher gibt es weder in der deutschen Grundwasserverordnung noch in der Trinkwasserverordnung einen Grenzwert für solche Stoffe.<br><br>Auch aus diesem Grund begrüßen wir den Vorschlag, die toxikologischen Risiken von Tierarzneimitteln für die Gesundheit und die Grundwasserökosysteme mittels einer Guidline zu regeln.<br><br>Wir bewerten den vorgeschlagenen Ansatz, eine Risikoabschätzung für prognostizierte Umwelt-Konzentrationen (PEC) von unter 0.1 µg/l durchzuführen(s. Szenario 2) grundsätzlich positiv.<br><br>ABER der Vorschlag zur Verfahrensänderung bei prognostizierter Umwelt-Konzentration (PEC) des Grundwassers von über 0.1 µg/l (s. Szenario 1) führt nach unserer Auffassung zu einer erheblichen Verschlechterung für den Umwelt- und Gesundheitsschutz und stellt eine Abkehr vom Vorsorgeprinzip dar! | |

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| | | Erklärung: Derzeit gilt: Eine im Rahmen der Zulassung prognostizierter Umwelt-Konzentration (PEC) des Grundwassers von über 0.1 µg/l gilt als nicht akzeptabel (S. Draft 56/57). Ein Antragssteller muss dann Risikominderungsmaßnahmen veranlassen. Reichen diese aus, den Wert auf unter 0.1 µg/l zu reduzieren, kann die Substanz zugelassen werden, reichen die Maßnahmen nicht aus, und bleibt eine PEC von über 0.1 µg/l bestehen, kann der Stoff nicht zugelassen werden. (Der Trinkwassergrenzwert im Grundwasser ist ein Ausschlusskriterium). Dies wird sich durch Szenario 1 ändern: Statt generell Belastungen von über 0.1 µg/l (PEC) nicht zu akzeptieren, soll das Risiko abgeschätzt werden (dies bedeutet, dass zukünftig für einige Stoffe auch PECs von weit über 0.1 µg/l plötzlich akzeptiert würden, sofern die ökotoxikologischen Daten für die Einzelsubstanz ein unakzeptables Risiko nicht erwarten lassen. (Nur Substanzen, die auch als Pestizid oder Biozid eingesetzt werden, sollen auf Grundlage des Vorsorgegrenzwertes von 0,1µg/l bewertet werden, da nicht ein und derselbe Wirkstoff unterschiedlich bewertet werden darf.) Die GRÜNE LIGA fordert, diese Änderung (Szenario 1) zu streichen.<br><br>Für viele Einzelsubstanzen existieren noch keinerlei ökotoxikologische Abschätzungen, häufig aus mangelndem Finanzierungswillen von politischer Seite. **Das Nicht-Vorhandensein von ökotoxikologischen Daten für alle zu überprüfenden Einzelsubstanzen darf kein** | |

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| | | **automatischer Zulassungsgarant werden**.<br><br>Weitere Kritikpunkte:<br><br>Mehrfachbelastungen, sogenannte „Medikamenten-Cocktails“, und Kombinationswirkungen von Einzelsubstanzen bleiben weiterhin unberücksichtigt. Selbst ein Unterschreiten der PEC von Einzelsubstanzen schließt nicht deren Schaden in Kombination aus.<br><br>Der Grundwasserschutz muss prioritär behandelt werden.<br><br>Eine Prüfung, ob es weniger stark umweltproblematische Arzneimittel gibt, erfolgt nicht. Dies ist ein Problem, denn zum Abschluss einer Bewertung folgt bei den Tierarzneimitteln stets eine Risiko-Nutzen-Analyse. Damit ist es möglich, selbst risikoreiche Mittel zuzulassen, wenn sie denn „nützlich“ genug sind. Die negativen Folgen werden der Allgemeinheit und zukünftigen Generationen aufgebürdet. An dieser Stelle wäre es daher notwendig, eine vergleichende Bewertung (wie bei Pestiziden und Bioziden) mit anderen Arzneimitteln durchzuführen, die für denselben Zweck eingesetzt werden: „Vergleichende Bewertung und Substitution“.<br><br>Wir plädieren für eine zentrale qualitative und quantitative Erfassung aller verabreichten Tierarzneimittel. Eine Erfassung der eingesetzten Mengen von Tierarzneimitteln findet bisher nicht statt und erschwert eine kontinuierliche Risiko- | |

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| | | Abschätzung.<br><br>**Wir appellieren an die EMA, das immissionsschutzrechtliche Minimierungsgebot (Vorsorgeprinzip) zu fördern**. Es müssen ein Monitoring zur Beobachtung der weiteren Entwicklung der Belastung in der Umwelt eingerichtet sowie längerfristig wirkende Strategien zur Minderung der Belastung entwickelt werden.<br><br>**Translation:**<br>In 2012, 1,619 tons of antibiotics were provided to veterinarians in Germany which corresponds to the two to threefold amount of antibiotics used in human medicine. Approximately 60 to 80% of the applied dose is excreted unchanged by the animals via faeces and urine, depending on the type of active substance, and enter soils via manure. At present no threshold value has been established, neither in the groundwater regulation nor in the German drinking water ordinance.<br><br>Therefore, we welcome the proposal of a guideline to regulate the toxicological risks posed by veterinary medicinal products to human health and groundwater ecosystems.<br><br>In principle we have a positive view of the proposed approach to perform a risk assessment for predicted environmental concentrations (PEC) of below 0.1 µg/l (s. scenario 2). | Thank you for your comment. |

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| | | HOWEVER, the proposal for procedural change for predicted environmental concentrations (PEC) of more than 0.1 µg/l (s. scenario 1) is for us leading to a substantial deterioration of health and environmental protection and constitute a move away from the precautionary principle.<br>Explanation: Currently in force: Predicted environmental concentrations (PEC) for groundwater above 0.1 µg/l are considered not acceptable (p. Draft 56/57). Risk mitigation measures have to be arranged by the applicant. If they are sufficient to reduce the concentration to a value below 0.1 µg/l, an authorisation can be granted; if they are not sufficient and the PEC groundwater remains above 0.1 µg/l, the authorisation can be refused. (The drinking water limit value for groundwater is an exclusion criterion). This will change with scenario 1: Instead of considering burden of more than 0.1 µg/l (PEC) generally unacceptable, a risk assessment shall be performed. This means that for some substances also PEC values considerably higher than 0.1 µg/ are suddenly acceptable, provided the data on ecotoxicity for the single substance do not indicate an unacceptable risk. (Only substances also used in biocides and plant protection products should be assessed on basis of the precautionary limit value of 0.1 µg/l, as the same substance must not be assessed differently.) The GRUENE LIGA requests the deletion of this change (scenario 1).<br><br>Data on ecotoxicity is lacking for many single substances, often due to insufficient willingness for financing from the | Not accepted. The purpose of this guideline was to move towards an environmental risk assessment based on a risk ratio approach (PEC/PNEC). |

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| | | political side. **The absence of ecotoxicological data for all substances to be assessed must not automatically become a guaranty for a marketing authorisation.** | Noted. Within the current framework on VMPs an ERA is needed for all new applications. |
| | | Additional critical issues:<br>Multiple stresses, so called 'medicines cocktails' and combination effects from single substances are still not considered. Even a short-fall of the PEC of single substances does not exclude adverse effects in combination. | Noted. Please refer to answer to comment 1, above regarding mixtures. |
| | | The protection of groundwater must be dealt with as a priority. An assessment as to whether pharmaceuticals with less adverse effects on the environment exists is not performed. This is a problem as for the final assessment of veterinary medicinal products a benefti-risk assessment is performed. This allows the marketing authorisation even for products with a high risk as long as they are 'beneficial' enough. The negative consequences are imposed on the general public and future generations. It would be necessary at this point to perform a comparative assessment (as for biocides and pesticides) with other pharmaceuticals for the same indication: 'Comparative assessment and substitution'. | Not accepted. Any environmental risks identified as a result of a Phase II assessment have to be considered within the benefit/risk balance of the product, bearing in mind that a risk to the environment can lead to the refusal to the authorisation of a product. We note the comment on comparative assessment; however this is outside the scope of this guideline. |
| | | We advocate a centralised qualitative and quantitative recording of all administered veterinary medicinal products. A recording of the administered amounts of veterinary medicinal products is not taking place at present which impedes a continuous risk assessment. | |

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| | | **We call upon the EMA to promote the immission control legal minimising obligation (precautionary principle).** A monitoring must be established to observe the further development of impacts on the environment as well as the development of long-term strategies for the reduction of the burden. | Noted.<br><br>Noted. |
| 17 | 18 | In principle we welcome the draft as a first constructive step in order to consider both human health and aquatic biota when realigning the risk assessment of veterinary pharmaceuticals relevant for groundwater.<br><br>At the same time we very much recommend to clarify the following important issues which are still unresolved:<br><br>• In order to reaffirm and be consistent with the precautionary principle and to prevent a deterioration of water bodies it should be clear that no pharmaceutical substance should exceed a concentration of 0,1 µg/l in groundwater regardless if a relevant substance is simultaneously listed and limited according to WFD Annex VIII 1-6 or GWD Annex I or not.<br><br>• Combination effects of pharmaceuticals should be | Thank you for your comment.<br><br>Noted. However the scope of this guideline was to move towards a risk assessment approach for groundwater.<br><br>Noted. Please refer to the answer to comment 1, |

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| | | considered as well. In this context, one should draw attention to a total 'sum' EQS/GQS like it is already established and applied for pesticides, biocides and its metabolites (cf. GWD Annex I). | above. |
| | | • Aquifers may be affected by several stressors, above all nitrate, pesticide and/or thermal pollution. Hence, it is recommended to establish a realistic scenario for assessing the effects of pharmaceuticals in groundwater ecosystems and to establish relevant requirements in the framework of the approval of active substances and veterinary medicinal products. | Not accepted. It is considered that the guideline has developed adequate methodology to quantify the risks from VMPs to human health and the environment. |
| | | • All data used for the approval procedure have to be available for the public. At present, they cannot be used for the deduction of EQS due to intellectual property rights. | Noted. However, this is outside the scope of this guideline. |
| | | • Veterinary pharmaceuticals should not be approved if they meet cut-off criteria established according to the pesticide and biocide regulation (Art. 5 Regulation EC No 1107/2009 and Art. 5 Regulation EU No 528/2012) or contradict to the principles according to Art. 4.1 b (= trend reversal), Art. 4.1 c (= achieving objectives of protected areas) and Art. 16.6 WFD (= phasing out of priority substances). | Not accepted. The framework for veterinary medicines requires a risk assessment for groundwater. This guideline was developed with the aim to provide scientific methodology to do so, and to characterise the risks based on the physciochemical and hazard properties of the substances. |
| | | • Veterinary pharmaceuticals, which accumulate in the | |

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| | | groundwater or occur in surface waters used for drinking water purposes have to be withdrawn from circulation. | Noted. The risk characterisation presented in the guideline considers PECgroundwater concentrations. If a substance would accumulate in the environment the PECgroundwater would increase and this which would be considered within the risk assessment and ultimately the benefit/risk balance of the product. If the substance would accumulate above PNEC values, such risks can lead to the refusal of the marketing authorisation. From human heath perspective, accumulation in groundwater would affect the PEGgw and thereby also the RQgw, and this is used to assess the risk to humans via drinking water. |

## 2. Specific comments on text

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| 18 | Title | 11 | Comments: The term ‘groundwater communities’ in the title is a little vague. Besides this, the term veterinary pharmaceuticals may be better replaced by veterinary medicinal products.<br><br>Proposed change: Guideline on assessing the environmental and human health risks of veterinary medicinal products in groundwater. | Accepted |
| 19 | 34 | 11 | Comments: human drinking water.<br><br>Proposed change: delete human. | Accepted |
| 20 | 35-36 | 11 | Comments: the scope is likely not ' a risk assessment of groundwater ' , etc. The phrasing groundwater for human health is also unlucky.<br><br>Proposed change :<br>This guideline provides a methodology for performing risk assessment of residues of veterinary medicinal products in groundwater, serving both as a source of drinking water and as an ecosystem. | Accepted |

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| 21 | 35-38 | 14 | Comment: I suggest adding the acronym of “veterinary medicinal products” at the bottom of the line 37.<br><br>Proposed change (if any): “This guideline provides a methodology for performing a risk assessment of groundwater for human health and aquatic ecosystems for veterinary medicinal products (VMPs).” | Accepted. |
| 22 | 37-38 | 2 | Comments: We explicitly reject introducing a risk assessment for any certain pharmaceutical substance having regard to a (predicted) pollution scenario above 0.1 µg/l unless validated test methods using typical groundwater organisms in environmentally realistic conditions are used.<br><br>Proposed change (if any): Withdraw this procedure. | Not accepted, there are no validated test methods using groundwater organisms. The PNEC groundwater is derived from PNEC surface water using an additional assessment factor. |
| 23 | 37-38 | 6 | We explicitly reject introducing a risk assessment for any certain pharmaceutical substance having regard to a (predicted) pollution scenario above 0.1 µg/l unless validated test methods using typical groundwater organisms in environmentally realistic conditions are used. | Thank you for your comment. Please refer to comment 22 above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change: Withdraw this procedure. | |
| 24 | 38-39 | 11 | Comments: highly mobile substance should be included here, as mobility (either alone or in combination with toxicity and/or persistency) renders them relevant to assess in this context.<br><br>Proposed change:<br>a risk assessment may be needed for highly toxic substances, and/or highly mobile and/or persistent substances in soil and subsurface environments. | Not accepted.<br>The mobility of a compound is considered when predictive models are applied and/or when Koc and DT50 in soil are considered (metamodel). High mobility means also high PECgroundwater value |
| 25 | 38-39 | 11 | Comments: Currently, the document only reports on the risk assessment for toxic VMPs, not on the risk assessment for persistent (and/or mobile, see comment above) VMPs.<br><br>Proposed change: Include risk assessment for substances that are persistent and/or mobile in the soil compartment, including an identification of those substances. | Thank you for your comment. Please see the answer to comment 24, above. |
| 26 | 40 | 4 | Comment: The sentence should read “This” guideline instead of “The”<br>Proposed change: “~~The~~This” | Agreed. |
| 27 | 49-52 | 4 | Comments: The sentence “*This guideline gives further technical support to the implementation of* | Partially agreed. The sentence has been changed in: “This guideline implement the VICH guidelines GL6 |

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| | | | *the 49 VICH guidelines GL6 (VICH 2000) and GL38 (VICH 2005) on the environmental risk assessment (ERA) 50 of VMPs*" is misleading as this guidance sets additional requirements beyond those given in the VICH guidelines<br><br>Proposed change: Please delete the sentence | (VICH 2000) and GL38 (VICH 2005) on the environmental risk assessment (ERA) of VMPs" |
| 28 | 52 | 11 | Comments: ' compare with' instead of 'compare against'<br><br>Proposed change:<br>change against into with | Accepted |
| 29 | 53 | 11 | Comments: The text reads: ' the value of 0.1 µg/L is the groundwater quality standard (GQS) for pesticides and biocides according to, etc.<br>The citation is incomplete, please add that the legal text (2006/118/EC) states ' Active substances in pesticides, including their relevant metabolites, degradation and reaction products'.<br>A footnote specifies the meaning of pesticides and biocide from their respective legislations (note: that have been updated since). We would like to stress the importance of this addition. The respective legislations cited (in their former version 91/414/EC and 98/8/EC as well as their | Accepted. |

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| | | | updates Regulations (EC) 1107/2009 and 528/2012, as amended) in Annex I of 2006/118/EC, contain cross reference to this limit with equal description (i.e. covering metabolites, degradation and reaction products) in the sections specifying how the risk assessment should be performed.<br><br>See for instance regulation 1107/2009 art 3 for definitions, where metabolites and breakdown products are specifically included for plant protection products.<br><br>Proposed change:<br>change for pesticides and biocides into<br>for pesticides and biocides including their relevant metabolites, degradation and reaction products | |
| 30 | 54 | 11 | Comments: this legal text was amended in 2014<br><br>Proposed change:<br>add: ' as amended'. | Partially agreed. Text re-drafted: “The value of 0.1 µg/l is the groundwater quality standard (GQS) for pesticides and biocides according to the Groundwater Directive 2014/80/EU Annex I, amending Directive 2006/118/EC (GWD). “ |
| 31 | 54 | 11 | Comments: Directive 98/83/EC is just as applicable as 2006/118/EC. The limit value for pesticides and their metabolites, degradation and reaction products applies. Please add reference to | Accepted. The sentence is re-phrased |

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| | | | this legal text.<br><br>Proposed change:<br>Add reference to Directive 98/83/EC. | |
| 32 | 56 | 11 | Comments: VMPs are meant here, not 'all substances'.<br><br>Proposed change:<br>Replace 'all substances' with VMPs.<br>Please check the document if the term substances is used in other cases where the term VMP would be more appropriate, in order to prevent unclarities. | Agreed. |
| 33 | 56 | 14 | Comment: I suggest not using a capital C in "Concentrations".<br><br>Proposed change (if any):concentrations | Agreed. |
| 34 | 56-62 | 11 | Comments: No reference is made to the situation where the concentration is equal to 0.1 µg/L.<br><br>Proposed change: Please check all references in the text regarding the use of the 0.1 µg/L limit, and adjust to 'higher than' or 'higher than or equal to' where appropriate. E.g., in the PPP | Agreed. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | framework it should read ‘higher than’. | |
| 35 | 57 | 11 | Comments: intrinsic hazardous properties. The word intrinsic is superfluous<br><br>Proposed change:<br>delete intrinsic | Accepted |
| 36 | 66 | 11 | Comments: interpreted by whom? CVMP or the groundwater legislation?<br><br>Proposed change: if it was as such interpreted by CVMP, the citation marks should be deleted and ‘by CVMP’ should be added. If it was as such interpreted within another framework, explicit reference should be made to this. | Partially accepted.<br>The PEC value has not to be interpreted; it is assumed as a not harmful value. |
| 37 | 72 | 15 | Comment: please explain the meaning of “safe concentration” as it confuses in this context. If “predicted” is meant please state as this. | Accepted. See our previous answer (the word safe has been changed) to comment number 1 |
| 38 | 72-73 | 11 | Comments: The last sentence of this section is understood. However, significantly can be removed here.<br><br>Proposed change:<br>delete significantly | Agreed. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| 39 | 78 | 11 | Comments: This Directive should be specified<br><br>Proposed change:<br>replace ' This Directive' with ' Directive 2006/118/EC, as amended' | Partially accepted. Text amended to 'The GWD'. |
| 40 | 80-81 | 4 | Comments: Comparing VMPs directly with pesticides and biocides may be inappropriate as VMPs are administered to an animal and not directly applied into the environment.<br><br>Proposed change: Please add <u>However most VMP's are not administered directly into the environment in the way that biocides and pesticides are, undergoing first a transit through the animal</u>. | Noted. |
| 41 | 85-88 | 11 | Comments: this sentence now reads as if the lack of assessment methodology was an omission in the guideline. However, this was not the case, since CVMP at that time did not accept concentrations above 0.1 µg/L (as mentioned in lines 56-60.<br><br>Proposed change: Delete or rephrase this sentence. | Accepted. The section has been clarified. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| 42 | 87 | 15 | Comment: please replice “where the predicted safe concentrations” by more appropriate regulatory wording<br><br>Proposed change (if any):”… for situations where the predicted no effect concentrations (PNEC) for the aquatic compartment are…” | Accepted |
| 43 | 90-91 | 11 | Comments: ' the safe annual average concentration' is a bit vague. Use appropriate wording.<br><br>Proposed change:<br>has revealed that the annual average environmental quality standard (AA-EQS) could be…etc. | Accepted |
| 44 | 91-92 | 4 | Comment: The UKTAG, 2012 report referred to is not retrievable (see also comment line 321-322), and seems rather outdated (https://www.wfduk.org/sites/default/files/Media/UKTAG_Technical%20report_GW_Haz-Subs_ForWebfinal.pdf ).<br><br>Proposed change: Please provide the correct reference. | Noted. Link was updated |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| 45 | 92-94 | 4 | Comments: Cypermethrin is a rather singled-out example. Is it appropriate to extrapolate an example of a pyrethroid used as a pesticide with direct application to crops to veterinary medicines, where there is a passage through an animal (which is also the case for cypermethrin)?<br><br>Proposed change: | Not accepted.<br>The cyperethrin serves as an example to show the difference in risk based approach in deriving EQS for surface waters and the arbitrary set GQS for pesticides in the groundwater. Different patterns of use (crops or animals) lead to different $PEC_{groundwater}$, while the toxic properties do not change. |
| 46 | 94 | 2 | “The taxa that are specifically sensitive to these kinds of compounds are also present in groundwater”<br><br>Comments: please specify, what is meant by “taxa”: is it specific taxonomic orders, e.g. “crustaceans”, or certain species?.<br><br>Proposed change (if any): | Accepted. Sentence has been rephrased. |
| 47 | 94 | 3 | “The taxa that are specifically sensitive to these kinds of compounds are also present in groundwater”.<br><br>Comments: please specify, what is meant by “taxa”: is it specific taxonomic orders, e.g. “crustaceans”, or certain species?). | Thank you for your comment. Please refer to the answer to comment 47, above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): | |
| 48 | 94 | 6 | “The taxa that are specifically sensitive to these kinds of compounds are also present in groundwater”.<br><br>Comments: please specify, what is meant by “taxa”: is it specific taxonomic orders, e.g. “crustaceans”, or certain species?. | Accepted. The taxa have been clarified. |
| 49 | 94 | 8 | “The taxa that are specifically sensitive to these kinds of compounds are also present in groundwater”.<br><br>Comment: please specify, what is meant by “taxa”: is it specific taxonomic orders, e.g. “crustaceans”, or certain species?).<br><br>Proposed change (if any): | Thank you for your comment. Please refer to the answer to comment 47, above. |
| 50 | 94-95 | 14 | Comment: true groundwater-dwelling organisms are not able to survive in surface water. Surface water organisms may be accidentally found in groundwater, however they do not thrive in this ecosystem. For these reason I suggest to modify the lines as following: | Thank you for your comment. Please refer to the answer to comment 47, above |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): The taxa that are specifically sensitive to these kinds of compounds have close phylogenetic relatives in groundwater. | |
| 51 | 98-111 | 2 | Comments: If it is said a compound should not enter der GW ecosystem at a concentration of ≥0.1µg/l, then in consequence the moment a concentration of 0.1µg/l is detected somewhere in groundwater distant to a potential entry point, the entry concentration must have been definitely higher. This should be excluded.<br><br>Proposed change (if any): | Not accepted<br>In a regulatory framework such as that of the authorization to market of chemicals the exposure is calculated through predictive models. For instance, for PPPs concentration of exposure and then risk is calculated “edge of the field” (meaning near one treated hectare and not somewhere distant to a potential entry point)<br>This is also true for FOCUS models that calculate PEC in groundwater 1 meter deep under the treated hectare area (one hectare).<br>The same approach is used for VMPs. In other words, we consider concentrations in GW derived from one hectare treated with a certain amount of manure containing VMPs. |
| 52 | 98-111 | 3 | Comments: If it is said a compound should not be present in GW ecosystem at a concentration of ≥0.1µg/l, then in consequence at that moment a concentration of 0.1µg/l is detected somewhere in groundwater distant to a potential entry point, the entry concentration must have been definitely higher. | Thank you for your comment. Please refer to the answer to comment 51, above |

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| | | | Proposed change (if any): | |
| 53 | 98-111 | 6 | Comments: If it is said a compound should not enter der GW ecosystem at a concentration of ≥0.1µg/l, then in consequence the moment a concentration of 0.1µg/l is detected somewhere in groundwater distant to a potential entry point, the entry concentration must have been definitely higher. This should be excluded.<br><br>Proposed change (if any): | Thank you for your comment. Please refer to the answer to the comment 51, above |
| 54 | 98-111 | 8 | CommentS: If it is said a compound should not enter der GW ecosystem at a concentration of ≥0.1µg/l, then in consequence the moment a concentration of 0.1µg/l is detected somewhere in groundwater distant to a potential entry point, the entry concentration must have been definitely higher.<br><br>Proposed change (if any): | Thank you for your comment. Please refer to the answer to the comment 51, above |
| 55 | 100-101 | 2 | Comments: We explicitly reject introducing a risk assessment for any certain pharmaceutical substance having regard to a (predicted) pollution scenario above 0.1 µg/l unless validated test methods using typical groundwater organisms in environmentally realistic conditions are used. | Thank you for your comment. Please refer to the answer to the comment 22, above. |

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| | | | Proposed change (if any): Withdraw this procedure. | |
| 56 | 101 | 15 | Comment: please change "… above the GQS of 0.1 µg/l." to "… equal or above the GQS of 0.1 µg/l." | Agreed. |
| | 103 | 11 | Comments: ' scientific evidence indicates' is strange wording as evidence is generally considered proof.<br><br>Proposed change:<br>'scientific data indicate' or 'experimental evidence indicates' | Agreed |
| 57 | 104 | 3 | Comments:<br><br>Proposed change (if any): Change "aquatic PNEC" to "$PNEC_{surfacewater}$" if applicable | Agreed. |
| 58 | 105 | 4 | Comments: Based on the aquatic effect studies, a PNEC for each water organism (algae, daphnia and fish) is calculated taking into account the toxicity endpoint divided by an appropriate assessment factor. How do you determine a $PNEC_{groundwater}$ for the ecosystems? The answer to | Not accepted. This paragraph is in the scope of the paper, where reference to specific chapters is not made. |

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| | | | this question is in § 5.2.<br><br>Proposed change (if any): Please refer to this paragraph | |
| 59 | 106-111 | 4 | Comment: This paragraph is subject to interpretation, and could imply that substances with a PNEC of e.g. 0.05 µg/L could enter groundwater up to concentrations of 0.099 µg/L.<br><br>Proposed change: please clarify. | Accepted. A sentence has been included at the end of the section to clarify this scenario. |
| 60 | 106-111 | 15 | It is appreciated that the draft guideline considers the European legislation on the protection of groundwater and relevant legislation addressing substances that are partially also used as veterinary medicines, such as pesticides or biocides. In line with the precautionary principle it is however questionable why 0.1 µg/l is an absolute quality standard for pesticides and biocides, but is not applied to other biologically active substances such as antibiotics. This partially contradicts article 6 of the groundwater Directive (2006/118/EC) which also considers for substances which are not classified as hazardous according to the Water Framework Directive (2000/60/EC), "*all measures necessary to limit* | Noted. |

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| | | | *inputs into groundwater so as to ensure that such inputs do not cause deterioration or significant and sustained upward trends in the concentrations of pollutants in groundwater*." | |
| 61 | 107 | 11 | Comments: consideration has to be given not only to (EU legislation on) groundwater, but also to that on drinking water. The introductory sections state that human health is part of the risk assessment. Groundwater is a drinking water source.<br><br>Proposed change:<br>add text: to relevant European Union legislation on groundwater and drinking water (add legislation references). | Accepted. |
| 62 | 107-111 | 9 | Comments: We support the initiative to include active substances of VMPs that are also used as pesticides and/or biocides to be subject to the same limits, as laid down in Annex II of the GWD.<br><br>But this does not go far enough in view of securing groundwater for future generations. Therefore we strongly suggest that all substances in VMPs – also those which are not identical to substances also used as pesticides and/or | The groundwater directive is outside the remit of the CVMP and that directive does not mention limits associated with VMPs. This guideline was developed in order to address this omission. |

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| | | | biocides - should be subject to the same limits.<br><br>Proposed change (if any):"In view of this, the CVMP considers that substances that come within the scope of points 1 to 6 of Annex VIII to the WFD, and active substances of VMPs that are also used as pesticides and/or biocides **and/or other active substances of VMPs** should be subject to the same limits, as laid down in Annex II of the GWD, i.e. that they should not enter groundwater at concentrations ≥ 0.1µg/l." | |
| 63 | 109 | 11 | Comments: pesticides and biocides..and their metabolites, degradation products and reaction products.<br><br>Proposed change:<br>add after pesticides and/or biocides and their relevant metabolites, degradation products and reaction products,… | Accepted. |
| 64 | 111 | 11 | Comment: '≥' should be 'above'<br><br>Replace with 'i.e., that leaching should not result in concentrations in groundwater above 0.1 ug/L'. | Partially agreed. Changed to equal or above. |
| 65 | 119 | 15 | Comment: The GDWQ was updated in 2017, this | Accepted. |

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| | | | version should be referred to: http://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/ | |
| 66 | 120 | 4 | Comments: In those exceptional cases where an ADI was not determined by the CVMP, what value should be used in the calculation?<br><br>Proposed change: please clarify. | The reason for that no ADI (or MRLs) has been established could be that the substance is of endogenous origin, constitutes a normal component in the human diet or that oral absorption is negligible etc., and therefore is not considered to pose a risk for consumers. This conclusion is valid also if the substance would enter the ground water, i.e. no $MTC_{dw}$ will be needed.<br><br>Substances for which no ADI (or MRLs) could be established, e.g. due to consumer relevant genotoxic carcinogenic effects, are not allowed in VMPs for food producing animals and will therefore not be subject for assessment of risk for humans via exposure from drinking water.<br><br>A clarification has been added. |
| 67 | 120 | 11 | Comments: use subscript for dw in equation. This is done in the text as well.<br><br>Proposed change:<br>consequent use of subscripts in parameter | Accepted. |

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| | | | definitions throughout document | |
| 68 | 124 | 11 | Comments: We propose the value of 70 kg, since this is the value used in the EU Water Framework Directive, using the same equation as equation 1, for the determination of water quality standards for sources of drinking waters. Moreover, the value of 60 kg body weight may be a good estimate world wide, but for the EU 70 kg body weight may be more appropriate.<br><br>Please note that the fraction of 0.1 of the ADI for the uptake via drinking water is in line with the EU WFD and should not be changed.<br><br>Proposed change: use 70 kg instead of 60 kg. | In MRL assessments a default body weight of 60 kg is used when calculating the theoretically maximal daily intake.<br><br>For consistency within CVMP GLs and not to underestimate the risk it is considered important to keep 60 kg as the default body weight.<br><br>MTCdw is to be calculated following the methodology used by the WHO. It is noted that the WHO uses up to 0.2 for P. However, for the evaluation of residues of veterinary medicines in groundwater in the EU an indicative value of 0.1 is considered adequate. The actual fraction of the ADI to be used for exposure via drinking water needs to remain flexible. This has been explained further in the text. |
| 69 | 125 | 11 | Comments: We strongly oppose to any product-based deviation from default values. Default values for body weight, the fraction of the ADI for uptake via drinking water and the daily consumption of drinking water are general values. These values do not change when another product is used. Thus whenever there is scientific evidence to change these values, they should be | Whereas the value used for body weight and daily consumption of drinking water should not deviate from the default values of 60 kg and 2l, respectively, the fraction of the ADI to be allocated to exposure via drinking water needs to be flexible, see the response to comment 68 above. |

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| | | | changed in the guideline, and not for single, specific products.<br><br>Proposed change: Delete asterisk and line 125. | |
| 70 | 128 | 11 | Comment: a reference for the WHO methodology is missing.<br><br>Proposed change: Add Reference for WHO methodology | Accepted. |
| 71 | 128-129 | 11 | See comment at line 125. When there is scientific justification for a change of default values, these should be changed in the guideline and not within product-based individual assessments. These default values are nót substance specific.<br><br>Proposed change: delete these lines. | Please see response to comment 69 above. |
| 72 | 133 | 3 | “It is recommended to operate with 10% as an indicative maximum percentage of the ADI to be used by drinking water.”<br><br>Comment: Please add reference.<br><br>Proposed change (if any): | Noted. However, the recommended approach is not based on a published reference. |

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| 73 | 133 | 11 | Comment: recommended by whom? CVMP?<br><br>Proposed change: add by whom this is recommended. Also add 'which is in line with the default value for the derivation of an EQS for drinking water sources within the EU WFD'. | Agree. Any deviations from the WHO guideline are explained. |
| 74 | 133-134 | 4 | Comments: There is no maximum limitation for any of the commodities in the standard food basket, and there is no justification why this should be the case for drinking water. The fraction available after calculation of the consumption of the food basket should be used in the equation, to ensure that total consumption plus drinking water does not exceed the ADI.<br><br>Proposed change: delete the maximum percentage. | The maximum fraction available for drinking water is not fixed. This is reflected in the text where it is stated that 0.1 is an indicative and flexible value. |
| 75 | 134-137 | 11 | See comment at line 125. When there is scientific justification for a change of default values, these should be changed in the guideline and not within product-based individual assessments. These default values are nót substance specific.<br><br>Proposed change: delete these lines. | Please see response to comment 69 above. |
| 76 | 136 | 14 | Comment: what does "MRLs" mean? This | Accepted |

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| | | | acronym should be explained the first time it occurs in the text. | |
| 77 | 138 | 4 | Comments: The VMP is not the concern- it is the active ingredient from the VMP, in particular if it is to be compared to the ADI which is based on the active ingredient not the VMP.<br><br>Proposed Change: "It is of paramount importance that the total intake of the active ingredient (from the VMP) by consumers" | Accepted |
| 78 | 140-148 | 4 | Comments: Before using this approach, the specific refinement (based on metabolism/manure and using Focus Pearl) will be performed in phase II Tier A and if the $PEC_{groundwater\ refined}$ is > 0.1 µg/L a risk assessment for human health should be performed and a $RQ_{gw}$ will be calculated. Therefore, could you specify what other refinement of the $PEC_{gw}$ could be performed at this step?<br><br>Proposed change: In lines 140 and 143, replace $PEC_{gw}$ in line 140 and 143 by $PEC_{gw\ refined}$.<br>In lines 114 to 148, delete the following sentences "This may include ~~a refinement of the PECgw and/or~~ a scientific justification for deviating from | Not agreed. The risk/ratio approach should be used based on the initial estimate of $PEC_{groundwater}$. Description of methods for refinement of $PEC_{groundwater}$ is considered to be out of scope of the current guideline. Reference to the CVMP TGD has been added. No other refinements than those described for Phase II Tier A in the CVMP TGD are implicated.<br><br>The proposal to change to $PEC_{ground\ water\ refined}$ and $RQ_{ground\ water\ refined}$ as appropriate is accepted. As the methods for refinement of $PEC_{groundwater}$ is considered to be out of scope of the current guideline the corresponding text has been deleted. |

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| | | | the default input parameters in the $MTC_{gw}$ calculation. ~~For a refinement and final establishment of the $PEC_{gw}$ the $K_{oc}$ and $DT_{50}$ are typically needed in order to run the appropriate models, which are available int e ERA according to the VICH GLs."~~ | |
| 79 | 144 | 4 | Comments: In case the RQ*gw* exceeds 1, a potential human safety risk has been identified in the context of this assessment, not a potential risk for groundwater.<br><br>Proposed change: Please correct: "In cases where the $RQ_{gw}$ exceeds 1.0 a potential human safety risk has been identified…." | Accepted |
| 80 | 144 | 15 | Comment: please replace "… exceeds 1.0 …" with "… reach or exceeds 1.0 …" as the value of 1.0 represents the trigger value.<br>Please delete "potential" as it might be an inappropriate and confusing wording related to the whole chapter. | Accepted |
| | 145-146 | 11 | See comment at line 125. When there is scientific justification for a change of default values, these should be changed in the guideline and not within product-based individual assessments. These default values are nót substance specific. | Please see response to comment 69 above |

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| | | | Proposed change: delete these lines. | |
| 81 | 146 | 4 | Comment: Typo between MTC dw and MTC gw<br><br>Proposed change: Line 146 should read MTCdw | Accepted |
| 82 | 148 | 4 | Comment: appropriate models are available in the CVMP TGD, not in the VICH GLs.<br><br>Proposed change: …which are available in ~~the ERA according to the VICH GLs~~ CVMP TGD. | Accepted |
| 83 | 151-154 | 2 | "In addition, because of the absence of primary producers in groundwater systems, the self purification process may be disturbed and the original state cannot be easily restored."<br><br>Comments: I do not quite understand how self-purification processes depend on primary production.<br><br>Proposed change (if any): "In addition, if the providers of key functions and processes are affected, the self-purification processes may be disturbed…" | Accepted. |
| 84 | 151-154 | 3 | "In addition, because of the absence of primary | Thank you for your comment. Please refer to the answer |

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| | | | producers in groundwater systems, the self-purification process may be disturbed and the original state cannot be easily restored."<br><br>Comments: I do not quite understand how self-purification processes depend on primary production.<br><br>Proposed change (if any): "In addition, if the providers of key functions and processes are affected, the self-purification processes may be disturbed…" | to comment 83, above. |
| 85 | 151-154 | 6 | "In addition, because of the absence of primary producers in groundwater systems, the self purification process may be disturbed and the original state cannot be easily restored."<br><br>Comments: Please clarify, how self-purification processes depend on primary production.<br><br>Proposed change (if any): "In addition, if the providers of key functions and processes are affected, the self-purification processes may be disturbed…" | Thank you for your comment. Please refer to the answer to comment 83, above. |
| 86 | 151-154 | 9 | "In addition, because of the absence of primary producers in groundwater systems, the self-purification process may be disturbed and the original state cannot be easily restored." | Accepted |

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| | | | Comments:<br><br>Proposed change (if any): "In addition~~, because of the absence of primary producers~~ in groundwater systems, the self-purification process may be disturbed and the original state cannot be easily restored **once the providers of key functions and processes are affected**." | |
| 87 | 152-153 | 14 | Comment: references are needed.<br>Proposed change (if any): Contamination of groundwater may permanently eradicate entire unique groundwater communities due to the low or absent ability to re-colonise any affected habitats (see for instance Di Lorenzo et al., 2015a,b).<br><br>Di Lorenzo T. et al., 2015a. Occurrence of volatile organic compounds in shallow alluvial aquifers of a Mediterranean region: Baseline scenario and ecological implications. Science of the Total Environment, 538: 712-723.<br><br>Di Lorenzo T. et al., 2015b. Ammonium threshold values for groundwater quality in EU may not protect groundwater fauna: evidence from an | Accepted. |

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| | | | alluvial aquifer in Italy. Hydrobiologia, 743: 139-150. | |
| 88 | 154 | 4 | Comments: Since primary producers are absent in groundwater, the endpoints for algae are not relevant, and the $PNEC_{groundwater}$ should be established based on studies with *Daphnia* and fish. This guideline should specify that.<br><br>Proposed change: Please specify in sections 4.2, 5.1.2 and 5.2 that algae are not relevant for groundwater assessment and that endpoints derived from *Daphnia* or fish, whichever is the most sensitive, are to be used to derive the $PNEC_{groundwater}$ | Not accepted.<br>For the protection of the whole groundwater compartment, it is also necessary to protect spring water where primary producers are present. |
| 89 | 154 | 8 | "In addition, because of the absence of primary producers in groundwater systems, the self purification process may be disturbed and the original state cannot be easily restored."<br><br>Comments: Scientifically it is not obvious that self-purification processes depend on primary production.<br>Proposed change (if any): "In addition, if the providers of key functions and processes are affected, the self-purification processes may be | Thank you for your comment. Please refer to the answer to comment 83, above. |

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| | | | disturbed…"<br><br>Proposed change (if any): | |
| 90 | 154 | 15 | Comment: please replace "absence of primary producers in groundwater systems" as there might be no logical link between primary producers and self-purification.<br><br>Proposed change (if any): "In addition, if key functions or associated processes are affected, the self-purification … " | Thank you for your comment. Please refer to the answer to comment 83, above |
| 91 | 154-155 | 11 | Comments: it reads ' because of the absence of primary producers in groundwater systems, the self-purification process may be disturbed'. In our view, micro-organisms are involved in the self-purifying process The oligotrophic conditions, low (sulfate reducing or methanogenic) redox potential and relatively low temperature (at shallow depth) make these communities vulnerable to disturbance and recovery may take a long time, if occurring at all.<br><br>Proposed change:<br>add wording to reflect the presence of micro-organisms, the oligotrophy and anoxic conditions | Partially accepted. Please see the answer to comment 83, above. |

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| | | | as conditions affecting the purification rate/capacity of subsurface environments | |
| 92 | 154-155 | 14 | Comment: here I cannot see the connection between primary producers and the self-purification process of a groundwater ecosystem, such as an alluvial aquifer, for instance. Although few, some studies are available on the role of groundwater microbes and metazoa in contaminants' removal. Groundwater microbes (such as bacteria, fungi, and protozoa) and stygofauna (macro- and meiofaunal invertebrates) provide important ecosystem services which support aquifer self-purification (see Kota et al., 1999; Marshall & Hall, 2004; Boulton et al., 2008). Sinton (1984) demonstrated an essential contribution of invertebrates in C turnover in a sewage-polluted aquifer. Microorganisms can oxidize organic pollutants to CO2 while reducing electron acceptors such as molecular oxygen, nitrate, metal oxides, or sulfate. Some other pollutants, such as chlorinated solvents, may serve as electron acceptors. Microbial biofilms coating the large interstitial surface areas of sediment particles are the main sites of | Partially accepted. Please see the answer to comment 83, above. |

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| | | | pollutants's biodegradation (Herzik et al., 2014). Microbial biofilms also provide food for grazing invertebrates (Bärlocher and Murdoch 1989). Microbial activity may be enhanced by this feeding activity (Danielopol 1989) as well as fuelled by nutrients excreted by groundwater invertebrates (Boulton 2000; Marshall and Hall 2004). Interstitial bacterial activity can also be increased by groundwater invertebrate bioturbation in finer sediments (Mermillod-Blondin et al. 2000) while invertebrate faeces potentially 'seed' the substrate with bacteria and themselves provide further substrate for microbial exploitation. | |
| 93 | 157-165 | 14 | Comment: I suggest mentioning hyporheic zones as well as other groundwater dependent ecosystems. Groundwater ecosystems are temporally or permanently water-saturated zones in the subsurface. They occur in unconsolidated sediments such as gravel and sand, or in karstified and fissured consolidated rocks such as caves, epikarst and phreatic zones. Groundwater ecosystems are flanked by important ecotones and by groundwater dependent ecosystems, commonly ranked on the basis of the degree of dependency on groundwater, such as the | Not accepted. The representative habitats were selected in order to define groundwater compartment. |

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| | | | hyporheic zone of rivers and streams, the interface to lentic water bodies such as lakes, the capillary fringe at the transition from the unsaturated (vadose) to the saturated zone and springs. | |
| 94 | 158 | 11 | Comments: It reads that following VICH guidelines, ecosystems in the aquatic compartment are defined by a few representative habitats, e.g. stream, pond, etc.<br>However, the VICH guidelines bases the assessment on a generic aquatic ecosystem and does not define specific habitats for aquatic environments. Accordingly, it is assumed that the ERA can be based on (generic) test species to represent this generic aquatic ecosystem.<br><br>Proposed change:<br>Rephrase using wording provided above. | Accepted. The text has been revised. |
| 95 | 160-165 | 2 | Comments: The selection of representative groundwater habitats is not complete, but springs as protected habitats are a good addition to this list. The hyporheic zone in streams might be a major entry path into groundwater, if water that is contaminated with VMPs is discharged into streams (e.g. due to insufficiently treated sewage | Not accepted. The representative habitats were selected in order to define groundwater compartment. |

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| | | | effluents).<br>Also, pastures and other agriculturally used areas with administration of VMPs may need to be considered, if they are located in aquifer recharge zones.<br><br>Proposed change (if any): “The most representative groundwater habitats are karstic, fractured and unconsolidated aquifers. For the protection of the whole groundwater compartment, it is necessary to consider and protect also alluvial gravel interstitial systems inclusive the hyporheic zone and spring water.” | |
| 96 | 160-165 | 6 | Comments: The selection of representative groundwater habitats is not complete, but springs as protected habitats are a good addition to this list. The hyporheic zone in streams might be a major entry path into groundwater, if water that is contaminated with VMPs is discharged into streams (e.g. due to insufficiently treated sewage effluents).<br>Also, pastures and other agriculturally used areas with administration of VMPs may need to be considered, if they are located in aquifer recharge zones. | Not accepted. Please see the answer to comment 95 above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): “The most representative groundwater habitats are karstic, fractured and unconsolidated aquifers. For the protection of the whole groundwater compartment, it is necessary to consider and protect also alluvial gravel interstitial systems inclusive the hyporheic zone and spring water.” | |
| 97 | 160-165 | 8 | Comments: The list of representative groundwater habitats considered is not complete, but we agree that springs need consideration. Others as well.<br>Proposed change (if any): The most representative groundwater habitats are karstic, fractured and unconsolidated aquifers. For the protection of the whole groundwater compartment, it is necessary to consider and protect also alluvial interstitial systems including the hyporheic zone and springs.<br><br>Also, pastures and other agriculturally used areas with administration of VMPs may need to be considered, if they are zones of significant groundwater recharge. | Not accepted. Please see the answer to comment 95 above. |
| 98 | 160-165 | 3 | Comments: The selection of representative groundwater habitats is not complete, but springs | Not accepted. Please refer to answer to comment 95 above. |

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| | | | as protected habitats are welcome in this list. The hyporheic zone in streams might be a major entry path into groundwater, if water that is contaminated with VMPs is discharged into streams (e.g. due to insufficiently treated sewage effluents).<br>Also, pastures and other agriculturally used areas with administration of VMPs may need to be considered, if they are located in aquifer recharge zones.<br><br>Proposed change (if any): “The most representative groundwater habitats are karstic, fractured and unconsolidated aquifers. For the protection of the whole groundwater compartment, it is necessary to consider and protect also alluvial gravel interstitial systems inclusive the hyporheic zone and spring water.” | |
| 99 | 170 | 15 | Comment: please avoid the term “safe concentration” in this context; it is inappropriate in the context of regulatory principles and approaches and is an incorrect term from an ecological point of view.<br><br>Proposed change (if any): use “predicted no effect concentration (PNEC)” or just “PNEC” if term and | Accepted |

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| | | | abbreviation are used above. | |
| 100 | 171 | 11 | Comments: ' from these three groups of organisms'<br>This can be made more explicit, as these organism groups are representatives of three trophic levels, on which the extrapolation from species to ecosystem is based; please include this term.<br><br>Proposed change:<br>Experimental data obtained for organisms from these three trophic levels….etc. | Accepted |
| 101 | 171-173 | 2 | Comments: Extrapolation from surface water situation to groundwater may be a first valid step, but must be definitely followed by the generation of reliable data from reliable tests. It's urgently required to conduct such tests with ecologically relevant organisms (e.g. amphipods from cold streams or stygophilous species like many copepods and crenobiont (spring) species) under realistic low temperatures.<br>It's hardly possible to conclude from tests with Daphnia und fish at > 20 °C to the reactions and behaviour of groundwater organisms living at 10 °C. The standard tests for surface water | Noted. Please refer to comment 1, above. |

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| | | | species (see test guidelines) are conducted under conditions which have nothing to do with groundwater environments.<br><br>Proposed change (if any): | |
| 102 | 171-173 | 3 | Comments: Extrapolation from surface water situation to groundwater may be a first valid step, but must be definitely followed by the generation of reliable data from reliable tests. It's urgently required to conduct such tests with ecologically relevant organisms (e.g. amphipods from cold streams, stygophilous species like many copepods or crenobionts) under realistic low temperatures. It's hardly possible to conclude from tests with Daphnia und fish at > 20 °C to the reactions and behaviour of groundwater organisms living at 10 °C. The standard tests for surface water species (see test guidelines) are conducted under conditions which have nothing to do with groundwater environments.<br><br>Proposed change (if any): | Noted. Please refer to comment 1, above. |
| 103 | 171-173 | 6 | Comments: Extrapolation from surface water situation to groundwater may be a first valid step, but must be definitely followed by the generation | Noted. Please refer to comment 1, above. |

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| | | | of reliable data from reliable tests. It's urgently required to conduct such tests with ecologically relevant organisms (e.g. amphipods from cold streams or stygophilous species like many copepods and crenobiont (spring) species) under realistic low temperatures.<br>It's hardly possible to conclude from tests with Daphnia und fish at > 20 °C to the reactions and behaviour of groundwater organisms living at 10 °C. The standard tests for surface water species (see test guidelines) are conducted under conditions which have nothing to do with groundwater environments. | |
| 104 | 171-173 | 8 | Comments: Extrapolation from surface water situation to groundwater may be a first valid step, but must be definitely followed by the generation of reliable data from reliable tests. It's urgently required to conduct such tests with ecologically relevant organisms (e.g. amphipods from groundwater or cold streams or stygophilous species like many copepods) under realistic low temperatures. It's hardly possible to conclude from tests with Daphnia und fish at > 20 °C to the reactions and behaviour of groundwater organisms living at 10 °C. The standard tests for surface water species are conducted under | Noted. Please refer to comment 1, above. |

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| | | | conditions distinct from groundwater environments.<br><br>Proposed change (if any): | |
| 104 | 171-173 | 14 | Comment: I am uncertain about this statement: "Experimental data obtained from these three groups of organisms [algae, daphnids and fish species] may be extrapolated to predict safe concentrations for highly adapted groundwater biota". The reason for my uncertainty is due to the complete absence of algae and daphnids in groundwater, and fish in European groundwater ecosystems. Groundwater-dwelling invertebrates are dominated by crustaceans belonging to several taxonomic groups but daphnids. Crustacea Copepoda is by far the most abundant and species-rich taxon in groundwater (Galassi et al. 2009; Di Lorenzo et al. 2013; Di Lorenzo and Galassi 2013). Epigean species can also be found, namely, stygoxenes, which enter groundwater occasionally or accidentally, however they are unable to reproduce in it. I agree with the fact that safe concentrations may be extrapolated from experimental data obtained from surface water taxa, however, if I may suggest, I would exclude algae and fish. | Not accepted.<br>Algae are primary producers which are present in spring ecotones consequently they must be taken into consideration<br>Daphnids are just taken in consideration as representative of invertebrates (exactly like in the case of surface waters)<br>Fish are present in spring ecotones and caves |

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| 105 | 172 | 11 | Comments: highly adapted groundwater biota this is not understood. Adapted to what? We presume to conditions in subsurface environments.<br><br>Proposed change:<br>change to 'groundwater biota highly adapted to subsurface environmental conditions and therefore vulnerable | Accepted |
| 106 | 172 | 15 | Comment: please see comment to line 170 | Noted |
| 107 | 174 | 3 | "Any additional uncertainties should be addressed through the use of more adequate assessment factors."<br><br>Comments: See comment above (regarding lines 171-173).<br><br>Proposed change (if any): "…should be addressed through the use of more adequate assessment factors, which however, on the long term, should eventually be displaced by reliable information gained from ecotoxicological studies performed with groundwater species and under realistic (i.e. groundwater-like) conditions". | Accepted |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| 108 | 174 | 6 | "Any additional uncertainties should be addressed through the use of more adequate assessment factors."<br><br>Comments: See comment above (regarding lines 171-173).<br><br>Proposed change (if any): "…should be addressed through the use of more adequate assessment factors, which however, on the long term, should eventually be displaced by reliable information gained from ecotoxicological studies performed with groundwater species and under realistic (i.e. groundwater-like) conditions". | Thanks for your comment. Please refer to the answer to comment 107, above. |
| 109 | 174 | 8 | "Any additional uncertainties should be addressed through the use of more adequate assessment factors."<br><br>Comments: I general, we agree to the comment above (regarding lines 171-173).<br>Proposed change (if any): "…should be addressed through the use of more adequate assessment factors, which however, on the long term, are displaced by reliable information gained from ecotoxicological studies performed with groundwater species and under realistic (i.e. groundwater-like) conditions". | Thanks for your comment. Please refer to the answer to comment 107, above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): | |
| 110 | 175 | 4 | Comment: What are “more adequate assessment factors”?<br><br>Proposed change: Please clarify | Accepted. |
| 111 | 187 and on | 11 | Comments: The titles of the paragraphs do not match the content of these paragraphs. We understand that the three bullets of the Millennium Assessment Report are followed, but this does not make the rationale in the text more understandable.<br><br>Proposed change: Change the headings of the paragraphs to better reflect the content of the paragraph. E.g., Exposure to toxicants in groundwater, Sensitivity of groundwater species to chemical stressors. The third heading is already changed. | Accepted |
| 112 | 188-193 | 14 | Comment: a further reason of prolonged exposure to stress is due to the low metabolism of groundwater taxa, that is significantly lower than the metabolism of close groundwater relatives. | Noted. |

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| 113 | 190 | 2 | "…groundwater ecosystems have a more prolonged period of exposure time, given that this ecosystem is generally colder than surface water systems…"<br><br>Comments: We assume, the authors mean that exposure times are longer, because biotic degradation processes (in terms of enzymatic reactions) take place more slowly under low temperatures as compared to higher temperatures? This should be explained more clearly, since otherwise it leads to confusion (as exposure times are also longer due to the low flow velocities in groundwater and the resulting long residence times, as stated later in the text.<br><br>Proposed change (if any): | Accepted. The text has been re-drafted for clarification. |
| 114 | 190 | 3 | "…groundwater ecosystems have a more prolonged period of exposure time, given that this ecosystem is generally colder than surface water systems…"<br><br>Comments: We assume, the authors mean that exposure times are longer, because biotic degradation processes (in terms of enzymatic reactions) take place more slowly under low temperatures as compared to higher temperatures? This should be explained more | Thanks for your comment. Please refer to the answer to comment 113, above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | clearly, since otherwise it leads to confusion (as exposure times are also longer due to the low flow velocities in groundwater and the resulting long residence times, as stated later in the text.<br><br>Proposed change (if any): | |
| 115 | 190 | 6 | "…groundwater ecosystems have a more prolonged period of exposure time, given that this ecosystem is generally colder than surface water systems…"<br><br>Comments: We assume, the authors mean that exposure times are longer, because biotic degradation processes (in terms of enzymatic reactions) take place more slowly under low temperatures as compared to higher temperatures? This should be explained more clearly, since otherwise it leads to confusion (as exposure times are also longer due to the low flow velocities in groundwater and the resulting long residence times, as stated later in the text.<br><br>Proposed change (if any): | Thanks for your comment. Please refer to the answer to comment 113, above. |
| 116 | 190 | 8 | "…groundwater ecosystems have a more prolonged period of exposure time, given that this ecosystem is generally colder than surface water systems…" | Thanks for your comment. Please refer to the answer to comment 113, above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Comments: We assume, the authors mean that exposure times are longer, because biotic degradation processes (in terms of enzymatic reactions) take place more slowly under low temperatures as compared to higher temperatures and higher microbial activities in surface waters? This should be explained more clearly, since otherwise it may lead to confusion (as exposure times are also longer due to the low flow velocities in groundwater and the resulting long residence times, as stated later in the text).<br><br>Proposed change (if any): | |
| 117 | 191 | 2 | "…complete absence of sunlight…could result in decreased biotic and abiotic degradation processes…"<br><br>Comments: why does the absence of sunlight lead to decreased degradation processes? Is photolytic degradation meant here? This should be stated more clearly.<br><br>Proposed change (if any): | Accepted. The text has been re-drafted for clarification. |
| 118 | 191 | 3 | "…complete absence of sunlight…could result in decreased biotic and abiotic degradation | Thanks for your comment. Please refer to the answer to comment 117, above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | processes…"<br><br>Comments: why does the absence of sunlight lead to decreased degradation processes? Is photolytic degradation meant here? This should be stated more clearly.<br><br>Proposed change (if any): | |
| 119 | 191 | 6 | "…complete absence of sunlight…could result in decreased biotic and abiotic degradation processes…"<br><br>Comments: why does the absence of sunlight lead to decreased degradation processes? Is photolytic degradation meant here? This should be stated more clearly.<br><br>Proposed change (if any): | Thanks for your comment. Please refer to the answer to comment 117, above. |
| 120 | 191 | 8 | "…complete absence of sunlight…could result in decreased biotic and abiotic degradation processes…"<br><br>Comments: Why does the absence of sunlight lead to decreased degradation processes? Is photolytic abiotic degradation meant here? This should be stated more clearly. | Thanks for your comment. Please refer to the answer to comment 117, above. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): | |
| 121 | 191 | 11 | Comments: groundwater systems are only colder than surface water systems in summer. This should be further specified. It could be added that the temperature of groundwater systems is usually rather constant (no seasonal influences).<br><br>Proposed change: see comment. | Noted. The groundwater maintains a constant temperature, whereas the temperature of surface water alters according to the surroundings |
| 122 | 191-192 | 11 | Comments: oligotrophy and low redox potential should be added here. They are very determining for large parts of groundwater bodies, albeit not all.<br><br>Proposed change:<br>add oligotrophy and low redox potential in this part of the text as determinants of decreased biotic degradation processes. | Accepted. |
| 123 | 194 | 11 | Comments: the residence time, for groundwater as well as for surface water, depends on the system's size.<br><br>Proposed change: Add reference for residence times in surface water. | Accepted. A reference was added |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| 124 | 197-199 | 9 | "Consequently, whereas the baseline quality of the riverine surface water may recover after a relatively short period of time, the recovery in aquifers (if any) may require decades, or disturbances may even be irreversible."<br><br>Comments: Groundwater is a valuable and vulnerable natural resource (see general comment). The evidence that disturbances may be irreversible is argument enough to explain why any contamination is unacceptable and must be prevented.<br><br>Proposed change (if any): "Consequently, whereas the baseline quality of the riverine surface water may recover after a relatively short period of time, the recovery in aquifers (if any) may require decades, or disturbances may even be irreversible. **Therefore any contamination is unacceptable.**" | Not accepted. How to address concentrations of VMPs in groundwater to consider their safety is the scope of this guideline. |
| 125 | 203-205 | 4 | Comments: What are "more adequate assessment factors"?<br><br>Proposed change: Please clarify | Thanks for your comment. Please refer to the answer to comment 107, above. |
| 126 | 204-205 | 14 | Comment: it is true that the chronic effects of | Noted. References have been considered. |

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| | | | chemical stressors to groundwater species have not been studied yet in laboratory due to the long life span of groundwater organisms. However, Di Lorenzo et al. (2014a) estimated the chronic lethality (CL) values and confidence intervals at 95% of the stygobiotic copepod species Diacylops belgicus exposed to several chemicals (ARIANE II, Urea, Ionized ammonia and Imazamox) using the Acute to Chronic Estimation method (ACE V3.0) according to Mayer et al. (1999). The results indicated that stygobitic species are likely much more sensitive to chemicals than their epigean relatives and that the CL under ARAINE II exposure was 0.2 µg/L for D. belgicus. Although these CL values were estimated from acute data, one of them proved to be reliable in a field experiment. Namely, Di Lorenzo et al. (2014b) found that groundwater copepods were significantly less abundant and less numerous in species in an aquifer sector where ionized ammonia concentrations were higher than the estimated CL value for D. belgicus (CL = 0.032 mg/L of ionized ammonia).<br><br>Di Lorenzo et al., 2014a. Sensitivity of hypogean and epigean freshwater copepods to agricultural pollutants. Environmental Science and Pollution | |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Research, 21(6): 4643-4655.<br><br>Di Lorenzo et al., 2014b. Ammonium threshold values for groundwater quality in the EU may not protect groundwater fauna: evidence from an alluvial aquifer in Italy. Hydrobiologia, 743(1): 139-150. | |
| 127 | 205 | 2 | Comments: see also Avramov et al. catecholamines<br>Avramov, M., Rock, T.M., Pfister, G., Schramm, K.-W., Schmidt, S.I. & Griebler, C.* (2013) Catecholamine levels in groundwater and stream amphipods and their response to temperature stress. General and Comparative Endocrinology 194: 110-117<br><br>Proposed change (if any): | Noted. |
| 128 | 205 | 3 | Comments: see also Avramov et al. catecholamines<br><br>Avramov, M., Rock, T.M., Pfister, G., Schramm, K.-W., Schmidt, S.I. & Griebler, C.* (2013) Catecholamine levels in groundwater and stream amphipods and their response to temperature stress. General and Comparative Endocrinology 194: 110-117 | Noted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): | |
| 129 | 205 | 6 | Comment: see also Avramov et al. catecholamines<br><br>Avramov, M., Rock, T.M., Pfister, G., Schramm, K.-W., Schmidt, S.I. & Griebler, C.* (2013) Catecholamine levels in groundwater and stream amphipods and their response to temperature stress. General and Comparative Endocrinology 194: 110-117<br><br>Proposed change (if any): | Noted. |
| 130 | 205 | 8 | Comments: You may also consider Avramov et al. catecholamines<br><br>Avramov, M., Rock, T.M., Pfister, G., Schramm, K.-W., Schmidt, S.I. & Griebler, C. (2013) Catecholamine levels in groundwater and stream amphipods and their response to temperature stress. General and Comparative Endocrinology 194: 110-117<br><br>Proposed change (if any): | Noted. |
| 131 | 205 | 11 | Comments: please clarify that 'species' in this | Accepted. This has been added as a footnote. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | context also means micro-organisms. This is not directly clear from the text, while in many subsurface environments, micro-organisms are likely to be the dominant biomass (both prokaryotic and eukaryotic micro-organisms).<br><br>Proposed change:<br>Add a sentence at the end of line 205. 'It is noted that species in the context of the groundwater compartment is understood to comprise micro-organisms or microbial communities. | |
| 132 | 206-210 | 14 | Comment: a reference should be replaced and another reference should be quoted.<br><br>Proposed change (if any): “Groundwater species have developed a number of metabolic adaptations for extreme energy saving to deal with starvation, for instance their metabolism is significantly lower than that of most other aquatic species (Di Lorenzo et al., 2015). These adaptations can affect the species response to a chemical stressor, and make them more sensitive to the long term effects of chemical stressors than surface water species (Di Lorenzo et al., 2014).”<br><br>Di Lorenzo, T., Di Marzio, W. D., Spigoli, D., | Accepted. |

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| | | | Baratti, M., Messana, G., Cannicci, S. and Galassi, D. M. P. 288 2015. Metabolic rates of a hypogean and an epigean species of copepod in an alluvial aquifer. 289 Freshw Biol, 60, 426–435.<br><br>Di Lorenzo, T., Di Marzio, W.D., Sáenz, M.E., Baratti, M., Dedonno, A.A., Iannucci, A., Cannicci., S., Messana, G., Galassi, D.M.P., 2014. Sensitivity of hypogean and epigean freshwater copepods to agricultural pollutants. Environ Sci Pollut Res 21: 4643-4655. | |
| 133 | 207 | 2 | "…their metabolism is significantly lower…"<br><br>Comments: to be precise, the metabolic rates (rather than the metabolism) are lower. Or: the metabolism is slower (rather than lower).<br><br>Proposed change (if any): change into "their metabolic rates are significantly lower" | Accepted. |
| 134 | 207 | 2 | Comments: In order to understand, why low metabolic rates can affect the species' response to a chemical stressor, it should be specified more clearly what the implications of this slow metabolism are: e.g. lower metabolic rates may include also lower depuration rates. | Accepted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): Add (Line 8) “Lower metabolic rates may include also lower depuration rates.” | |
| | 207 | 3 | “…their metabolism is significantly lower…”<br><br>Comments: to be precise, the metabolic rates (rather than the metabolism) are lower. Or: the metabolism is slower (rather than lower).<br><br>Proposed change (if any): change into “their metabolic rates are significantly lower” | Thanks for your comment. Please see the answer to comments 133 and 134 above |
| 135 | 207 | 3 | Comments: In order to understand, why low metabolic rates can affect the species’ response to a chemical stressor, it should be specified more clearly what the implications of this slow metabolism are: e.g. lower metabolic rates may include also lower depuration rates.<br><br>Proposed change (if any): Add (Line 8) “Lower metabolic rates may include also lower depuration rates.” | Thanks for your comment. Please see the answer to comments 133 and 134 above |
| 136 | 207 | 6 | “…their metabolism is significantly lower…”<br><br>Comments: to be precise, the metabolic rates (rather than the metabolism) are lower. Or: the | Thanks for your comment. Please see the answer to comments 133 and 134 above |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | metabolism is slower (rather than lower).<br><br>Proposed change (if any): change into “their metabolic rates are significantly lower” | |
| 137 | 207 | 6 | Comments: In order to understand, why low metabolic rates can affect the species’ response to a chemical stressor, it should be specified more clearly what the implications of this slow metabolism are: e.g. lower metabolic rates may include also lower depuration rates.<br><br>Proposed change (if any): Add (Line 8) “Lower metabolic rates may include also lower depuration rates.” | Accepted. |
| 138 | 207 | 8 | “…their metabolism is significantly lower…”<br><br>Comments: to be precise, the metabolic rates (rather than the metabolism) are lower. Or: the metabolism is slower (rather than lower).<br><br>Proposed change (if any): change into “their metabolic rates are significantly lower” | Thanks for your comment. Please see the answer to comment above of stakeholder 2 and 3 |
| 139 | 207 | 8 | Comments: In order to understand why low metabolic rates can affect the species’ response to a chemical stressor, it should be specified more | Accepted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | clearly what the implications of this slow metabolism are: e.g. lower metabolic rates may include also lower depuration rates. | |
| 139 | 207 | 11 | Comments: 'their metabolism is lower'. This should read: their rate of metabolism is lower.<br><br>Proposed change:<br>rate of metabolism is lower instead of metabolism is lower. | Thanks for your comment. Please see the answer to comment above of stakeholder 2 and 3 |
| 140 | 210 | 2 | “However, it is also important to note that the metabolic potential of groundwater species under sudden favourable conditions is higher for faster energy recovery and restoration of body reserves ”<br><br>Comments: Why is this important to note? What are the implications of this fact in terms of sensitivity to toxic chemicals?.<br>The implications should be stated more clearly:<br><br>Proposed change (if any): Add: “Faster restoration of body reserves may lead to higher uptake rates of lipophilic substances and storage in fatty tissues.<br>Otherwise (if not added) the sentence should be deleted as it does not support the line of | Accepted |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | argument. | |
| 141 | 210 | 3 | “However, it is also important to note that the metabolic potential of groundwater species under sudden favourable conditions is higher for faster energy recovery and restoration of body reserves ”<br><br>Comments: Why is this important to note? What are the implications of this fact in terms of sensitivity to toxic chemicals?.<br>The implications should be stated more clearly:<br><br>Proposed change (if any): Add: “Faster restoration of body reserves may lead to higher uptake rates of lipophilic substances and storage in fatty tissues.<br>Otherwise (if not added) the sentence should be deleted as it does not support the line of argument. | Thanks for your comment. Please see the answer to comment above of stakeholder 2<br><br>Accepted. The proposed sentence has been included. |
| 142 | 210 | 6 | “However, it is also important to note that the metabolic potential of groundwater species under sudden favourable conditions is higher for faster energy recovery and restoration of body reserves ” | Accepted. The proposed sentence has been included. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Comments: Why is this important to note? What are the implications of this fact in terms of sensitivity to toxic chemicals?.<br>The implications should be stated more clearly:<br><br>Proposed change (if any): Add: “Faster restoration of body reserves may lead to higher uptake rates of lipophilic substances and storage in fatty tissues.<br>Otherwise (if not added) the sentence should be deleted as it does not support the line of argument. | |
| 143 | 210 | 8 | “However, it is also important to note that the metabolic potential of groundwater species under sudden favourable conditions is higher for faster energy recovery and restoration of body reserves ”<br><br>Comments: Why is this important to note? (What are the implications of this fact in terms of sensitivity to toxic chemicals?).<br><br>Proposed change (if any): The implications should be stated more clearly (I assume: faster restoration of body reserves may lead to higher uptake rates of lipophilic substances and storage | Accepted. The proposed sentence has been included. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | in fatty tissues?). Otherwise the sentence should be deleted as it does not support the line of argument. | |
| 144 | 217 | 2 | "…lower levels of complexity…"<br><br>Comments: What do the authors mean here? Lower number of trophic levels/ shorter food chains? This should be stated more clearly in order to better understand the next sentences. This also reveals another important aspect: the biomagnification along trophic chains.<br><br>Proposed change (if any): Change to "lower levels of complexity (in terms of a lower number of trophic levels) due to the allotrophy and heterotrophy…" | Accepted. |
| 145 | 217 | 3 | "…lower levels of complexity…"<br><br>Comments: What do the authors mean here? Lower number of trophic levels/ shorter food chains? This should be stated more clearly in order to better understand the next sentences. This also reveals another important aspect: the biomagnification along trophic chains. | Accepted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): Change to “lower levels of complexity (in terms of a lower number of trophic levels) due to the allotrophy and heterotrophy…” | |
| 146 | 217 | 6 | “…lower levels of complexity…”<br><br>Comments: What do the authors mean here? Lower number of trophic levels/ shorter food chains? This should be stated more clearly in order to better understand the next sentences. This also reveals another important aspect: the biomagnification along trophic chains.<br><br>Proposed change (if any): Change to “lower levels of complexity (in terms of a lower number of trophic levels) due to the allotrophy and heterotrophy…” | Accepted. |
| 147 | 217 | 8 | “…lower levels of complexity…”<br><br>Comments: What do the authors mean here? Lower number of trophic levels/ shorter food chains? This should be stated more clearly in order to better understand the following sentences. This also reveals another important aspect: the accumulation and biomagnification along trophic chains. | Accepted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): Change to “lower levels of complexity (in terms of a lower number of trophic levels) due to the allotrophy and heterotrophy…” | |
| 148 | 218 | 2 | “This lower levels of complexity also implies that re-colonisation after perturbation may be extremely slow”<br><br>Comments: What do the authors mean here? Why does re-colonisation depend on a low or high complexity?<br><br>Proposed change (if any): this needs to be explained | Not accepted. A reference is already included. |
| 149 | 218 | 3 | “This lower levels of complexity also implies that re-colonisation after perturbation may be extremely slow”<br><br>Comments: What do the authors mean here? Why does re-colonisation depend on a low or high complexity?<br>Does it mean “lower abundances of species in migratable distance, or lower number of trophic levels - less competitors and predators”? | Not accepted. A reference is already included. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): this needs to be explained | |
| 150 | 218 | 6 | "This lower levels of complexity also implies that re-colonisation after perturbation may be extremely slow"<br><br>Comments: What do the authors mean here? Why does re-colonisation depend on a low or high complexity?<br><br>Proposed change (if any): this needs to be explained | Not accepted. A reference is already included. |
| 151 | 218 | 8 | "This lower levels of complexity also implies that re-colonisation after perturbation may be extremely slow"<br><br>Comments: What do the authors mean here? Why does re-colonisation depend on a low or high complexity? This awaits to be explained better. See also comment to Line 224. | Not accepted. A reference is already included. |
| 152 | (2018-2010) | 14 | Comments: I suggest adding a reference of a paper dealing with the effect of earthquakes on groundwater biota. Although the study that I'm suggesting does not deal with pollutants, it provides a strong evidence that a dramatic disturbing event (as an earthquake but also as a contamination event) may irreversibly decrease | Not accepted. The reference is not considered adequate for this guideline. Additionally, a new paragraph has been added at the end of this section to address this aspect better. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | subterranean species abundance, crashing populations' turnover rates. Groundwater communities are notorious for their low resilience. Therefore, any major disturbance that negatively impacts survival or reproduction may lead to local extinction of species,<br>most of them being the only survivors of phylogenetic lineages extinct at the Earth surface.<br><br>Proposed change (if any): This lower level of complexity also implies that re-colonisation after perturbation may be extremely slow, and that the restoration of an affected biotic community is unlikely (Culver and Pipan, 2009; Galassi et al., 2014).<br><br>Galassi, D.M.P., Lombardo, P., Fiasca, B., Di Cioccio, A., Di Lorenzo, T., Petitta, M., Di Carlo, P.,, 2014. Scientific Reports, 4: 6273. | |
| 153 | 221 | 2 | "Groundwater species are characterised by a high level of endemism"<br><br>Comments: a species does not have a level of endemism (it is either endemic or not).<br><br>Proposed change (if any): Change into "Groundwater communities are characterised by a high level of endemism" | Accepted |
| 154 | 221 | 3 | "Groundwater species are characterised by a high level of endemism" | Accepted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Comments: a species does not have a level of endemism (it is either endemic or not).<br><br>Proposed change (if any): Change into "Groundwater communities are characterised by a high level of endemism" | |
| 155 | 221 | 6 | "Groundwater species are characterised by a high level of endemism"<br><br>Comments: a species does not have a level of endemism (it is either endemic or not).<br><br>Proposed change (if any): Change into "Groundwater communities are characterised by a high level of endemism" | Accepted. |
| 156 | 221 | 8 | "Groundwater species are characterised by a high level of endemism"<br><br>Comments: A species does not have a level of endemism (it is either endemic or not).<br><br>Proposed change (if any): Change into "Groundwater communities are characterised by a high level of endemism" or "Groundwater communities are | |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | characterised by a high portion of endemic species" | |
| 157 | 221-222 | 14 | Comments: a reference is needed.<br>Proposed change (if any): Groundwater species are characterised by a high level of endemism, longevity, slow growth and low reproduction rates (Gibert et al., 1994).<br><br>Gibert, J., Danielopol, D.L., Stanford, J.A., 1994. Groundwater Ecology. Academic Press, Inc. | Accepted. |
| 158 | 224 | 2 | "Surface water ecosystems are characterised by a higher level of complexity, making them more able to recover from stress"<br><br>Comments: What do the authors mean here? (Why does a higher level of complexity lead to a faster recovery?) Is it the functional redundancy (i.e. more species are available to fulfil the same function, as compared to groundwater ecosystems)?<br>Or is it the higher connectivity to other habitats that allows a faster re-colonization of disturbed areas by organisms coming from nearby, undisturbed areas? (But the latter is not related to the low level of complexity due to allotrophy and heterotrophy). This needs to be explained more clearly. Other aspects of groundwater ecosystems which are also important and might be added in this line of argument are the following: | Accepted |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | Proposed change (if any): “On the other hand, groundwater ecosystems display particularities, which hinder re-colonization:<br>- groundwater species usually have a very low mobility (e.g. no drifting behaviour is possible as in streams), so that recolonization of disturbed areas from undisturbed neighbour areas is very difficult and slow<br>- groundwater is strongly fragmented, thus many aquifers may have a low connectivity with others<br>- groundwater organisms have very low reproduction rates, which leads to very slow recovery of populations after disturbance” | |
| 159 | 224 | 3 | “Surface water ecosystems are characterised by a higher level of complexity, making them more able to recover from stress”<br><br>Comments: What do the authors mean here? (Why does a higher level of complexity lead to a faster recovery?) Is it the functional redundancy (i.e. more species are available to fulfil the same function, as compared to groundwater ecosystems)?<br>Or is it the higher connectivity to other habitats that allows a faster re-colonization of disturbed areas by organisms coming from nearby, | Accepted. |

| | Line no. | Stakeholder no. | Comment and rationale; proposed changes | Outcome |
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| | | | undisturbed areas? (But the latter is not related to the low level of complexity due to allotrophy and heterotrophy). This needs to be explained more clearly. Other aspects of groundwater ecosystems which are also important and might be added in this line of argument are the following:<br><br>Proposed change (if any):<br>“On the other hand, groundwater ecosystems display particularities, which hinder re-colonization:<br>- groundwater species usually have a very low mobility (e.g. no drifting behaviour is possible as in streams), so that recolonization of disturbed areas from undisturbed neighbour areas is very difficult and slow<br>- groundwater is strongly fragmented, thus many aquifers may have a low connectivity with others<br>- groundwater organisms have very low reproduction rates, which leads to very slow recovery of populations after disturbance” | |
| 160 | 224 | 6 | “Surface water ecosystems are characterised by a higher level of complexity, making them more able to recover from stress”<br><br>Comments: What do the authors mean here? (Why does a higher level of complexity lead to a | Accepted. |

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| | | | faster recovery?) Is it the functional redundancy (i.e. more species are available to fulfil the same function, as compared to groundwater ecosystems)?<br>Or is it the higher connectivity to other habitats that allows a faster re-colonization of disturbed areas by organisms coming from nearby, undisturbed areas? (But the latter is not related to the low level of complexity due to allotrophy and heterotrophy). This needs to be explained more clearly. Other aspects of groundwater ecosystems which are also important and might be added in this line of argument are the following:<br><br>Proposed change (if any):<br>“On the other hand, groundwater ecosystems display particularities, which hinder re-colonization:<br>- groundwater species usually have a very low mobility (e.g. no drifting behaviour is possible as in streams), so that recolonization of disturbed areas from undisturbed neighbour areas is very difficult and slow<br>- groundwater is strongly fragmented, thus many aquifers may have a low connectivity with others<br>- groundwater organisms have very low reproduction rates, which leads to very slow recovery of populations after disturbance” | |

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| 161 | 224 | 8 | “Surface water ecosystems are characterised by a higher level of complexity, making them more able to recover from stress”<br><br>Comments: What do the authors mean here? (Why does a higher level of complexity lead to a faster recovery?) Is it the functional redundancy (i.e. more species are available to fulfil the same function, as compared to groundwater ecosystems)?<br>Or is it the higher connectivity to other habitats that allows a faster re-colonization of disturbed areas by organisms coming from nearby, undisturbed areas? (But the latter is not related to the low level of complexity due to allotrophy and heterotrophy).<br><br>Proposed change (if any): This needs to be explained more clearly. Other aspects of groundwater ecosystems which are also important and might be added in this line of argument are the following:<br>- in alluvial aquifers, groundwater species have a very low mobility (e.g. no drifting behaviour is possible as in streams), so that recolonization of disturbed areas from undisturbed neighbour areas is very difficult and slow | Accepted. |

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| | | | - some habitats in aquifers may have a low connectivity with others<br>- groundwater organisms have very low reproduction rates, which leads to very slow recovery of populations after disturbance | |
| 162 | 227 | 11 | Comments: a realistic time frame<br>what is 'realistic' in relation to recovery? Could this e.g. be coupled to duration of a leaching event (months–years)?<br><br>Besides, recovery is not taken into account in the assessment procedure for VMPs (in contrast to PPPs, where recovery within a defined time frame is a higher tier option part of the assessment).<br><br>Proposed change:<br>indicate length of timeframe envisaged; rephrase this paragraph. | Accepted. A reference has also been added. |
| 163 | 230 | 11 | Comments: ' the arguments presented above show that groundwater ecosystems may be more vulnerable than surface water ecosystems'.<br>In our opinion, the arguments given does not show that a higher vulnerability is anticipated. It is clear however, that once perturbed, most groundwater communities are likely to recover | Partially accepted. Additional text has been added that explain the reasons of slower re-colonisation for groundwater communities. |

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| | | | with much more difficulty. Whether or not the species themselves are more sensitive to toxic effects of xenobiotic substances, has not been shown. More scientific arguments for the latter should be provided.<br><br>Besides this, in this paragraph the precautionary principle, 'no anthropogenic substances in groundwater' could be added.<br><br>Proposed change:<br>rephrase ' show that groundwater systems may be more vulnerable' . Add sentence on precautionary principle. | |
| 164 | 230-233 | 4 | Comments: Bulog and Bizjak describe the remarkable bioaccumulation and tolerance of a salamander species for e.g. PCBs, zinc and arsenic; the authors indicate that the ability of Proteus to survive the high loads of contaminants accumulated in its tissues deserves further study. Culver and Pipan describe the biology of caves and other subterranean habitats.<br>Collectively (also see comment on lines 203-205) these references do not provide scientific support for an additional assessment factor of 10 on the PNEC for surface water. It seems that natural | Noted. Please refer to the answer to comment 1 above with regards to the choice of an additional assessment factor. |

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| | | | phenomena can be more detrimental to groundwater species.<br><br>Proposed change: Please provide scientific evidence supporting the use of an additional safety factor, certainly since it has been shown in the frame of the WFD and GWD that surface water PNECs are protective for groundwater species, or delete the requirement for the additional factor. | |
| 165 | 230-233 | 9 | "The arguments presented above show that groundwater ecosystems may be more vulnerable than surface water ecosystems and may lack the ability to recover from perturbations. As a result, an additional assessment factor of 10 should be applied to extrapolate the PNEC groundwater from the PNEC Surfacewater."<br><br>Comments:<br>A) We welcome the intention of considering the specific vulnerability of groundwater and to compensate for the uncertainty of extrapolation from test systems made for surface water situations to groundwater (with different relevant organisms and temperature) by introducing an uncertainty-factor 10. But would like to | Not accepted. The text already states that 'an additional assessment factor of 10….". It is considered the paragraph is sufficiently clear. |

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| | | | stress out that this can only be an interim solution until tailored standard tests for groundwater communities are in place.<br>B) The text does not explain that there is already a factor of 100 in place and that the factor of 10 is additional. We propose that this is clarified in the paragraph.<br><br>Proposed change (if any): - | |
| 166 | 232 | 2 | ”As a result, an additional assessment factor of 10 should be applied to extrapolate the PNECgroundwater from the PNECSurfacewater”<br><br>Comments: this is an important first step, until ecotoxical data from groundwater will be available. Specific research is urgently required!<br><br>Proposed change (if any): Add ” Surfacewater, until ecotoxicological data from groundwater will be available”. | Accepted |
| 167 | 232 | 3 | ”As a result, an additional assessment factor of 10 should be applied to extrapolate the PNECgroundwater from the $PNEC_{Surfacewater}$”, | Accepted |

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| | | | Comments: this is an important first step, until ecotoxical data from groundwater will be available. Specific research is urgently required!<br><br>Proposed change (if any): Add " $_{Surfacewater,}$ until ecotoxicological data from groundwater will be available". | |
| 168 | 232 | 6 | "As a result, an additional assessment factor of 10 should be applied to extrapolate the PNECgroundwater from the PNECSurfacewater",<br><br>Comments: this is an important first step, until ecotoxical data from groundwater will be available. Specific research is urgently required!<br><br>Proposed change (if any): Add " Surfacewater, until ecotoxicological data from groundwater will be available". | Accepted |
| 169 | 232 | 8 | Comments: This is an important first step, until groundwater-specific ecotoxicological data will be available. Specific research is urgently required!<br>Proposed change (if any): As a result, an additional assessment factor of 10 should be applied to extrapolate the PNECgroundwater from the $PNEC_{Surfacewater,}$ until ecotoxicological data from groundwater will be available. | Accepted |

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| 170 | 232 | 11 | Comments: Within the WFD framework (citing REACH), the extra assessment factor of 10 for the marine PNEC is substantiated with the reasoning that the greater species diversity of marine waters as opposed to freshwaters may mean that the distribution of sensitivities is broader, which has warranted an increased assessment factor (see REACH see R.10.3.2.1, page 24). This implicitly suggests that the unknown sensitivity of these extra marine species means that some of these species are more sensitive than the species for which the sensitivity is known. The arguments vulnerability, complexity and limited data are not used to substantiate the extra AF of 10 for the marine compartment.If the authors intend to apply the same argument for an extra AF of 10 to the groundwater ecosystems, to underpin a higher assessment factor, this assumption should be made explicit. If the reasoning is different, this should be made clear.<br><br>We note that it is not correct to refer to the WFD (2013/39/EU) legal text. The rationale is not contained in there, but in the technical guidance document for EQS derivation, which actually refers to REACH guidance for underlying | Partially accepted. The additional use of an AF of 10 is considered in the basis of vulnerability of the system. The reasoning is presented in sections 4.2.1, 4.2.2, 4.2.3. The text is thein these sections have been updated for clarity. The conclusion (4.2.4) mentions that the added AF of 10 is the result of the vulnerability of this ecosystem.<br><br>Reference to TG for deriving EQS has been added. |

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| | | | argumentation.<br><br>Proposed change:<br>Remove the reference to the WFD legal text to underpin the extra factor of 10.<br>Use wording applicable to groundwater, to underpin the extra AF of 10 (why not another value?) based on a known greater diversity of species in groundwater ecosystems, rather than copying the rationale employed for marine water from WFD/REACH. If this cannot be substantiated, rephrase text accordingly. | |
| 171 | 233 | 3 | Comments: $PNEC_{surrfacewater}$ → deleate one"r" | Accepted |
| 172 | 237 | 11 | Comments: use of the parameter $PNEC_{surface\ water}$.<br><br>The CVMP ERA framework does not define an overall $PNEC_{surface\ water}$. According to CVMP/VICH/790/03-FINAL, on the outcomes of the toxicity tests with species of each of the three trophic levels (primary producers, primary consumers, secondary consumers), an individual assessment factor is applied. This gives three separate PNECs based on the different taxonomic groups (section 3.1.3.2 VICH Phase II and also further sections, e.g. Figure 1) that are then all | Accepted. Sentence has been rephrased adding details on how to derive $PNEC_{surfacewater}$ |

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| | | | used in the ERA, although the ERA is usually only continued for the most critical PNEC. However, the PNECs remain explicitly calculated for each taxonomic level individually, they are not defined as $PNEC_{surface\ water}$. Hence, in this groundwater guidance, this term should be replaced by e.g. ' the most critical PNEC for the surface water compartment.'<br><br>Proposed change:<br>The text should be adapted; delete $PNEC_{surface\ water}$. It could be an option to select the lowest appropriate PNEC for an aquatic trophic level. | |
| 173 | 237 | 15 | The use of an additional assessment factor of 10 is supported as no test systems for groundwater species are available yet and because of the specific situation in groundwater described in chapter 4.2.<br>Additional uncertainties exists with regards to cumulative effects of mixtures which should be addressed (please consider Han and Price, 2011, Int. J. Environ. Res. Public Health 2011, 8(12), 4729-4745 „Determining the Maximum Cumulative Ratios for Mixtures Observed in Ground Water Wells Used as Drinking Water Supplies in the United States“). | Thank you for your comment. The reference has not been included, as the issue of mixtures is not only specific for groundwater systems, and section 4.2 tries to highlight those aspects that specifically differ between groundwater and surface water ecosystems. |

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| 174 | 238 | 2 | Comments:<br>Here, in chapter 5 of this draft, other ecotoxicological test should be named, in particular those, which are known to react sensitive to antibiotica and antiparasitica, e.g.:<br>- ecologically relevant organisms (e.g. Amphipods from cold streams or stygophilous species like many copepods) under realistic low temperatures.<br>- Bacteria: Pseudomonas, Ames (TA 100 und 98), umu-Test<br>- Algae<br>- Makrophytes: *Myriophyllum aquaticum* (?)<br>- Fish: Fish egg- test, Early-Life-Stage, Fish embryo-Acute-Toxicicty (because these are the most vulnerable stages)<br>- Mouse-Lymphoma-test<br><br>Proposed change (if any): | Not accepted. The guideline has been prepared in line with the VICH guidelines 6 and 38 and tests recommended in these guidelines, which are the ones internationally agreed for veterinary pharmaceuticals. |
| 175 | 238 | 3 | Comments:<br>Here, in chapter 5 of this draft, other ecotoxicological test should be named, in particular those, which are known to react sensitive to antibiotica and antiparasitica. Such tests could be applied to generate ecotoxicological information for groundwater taxa:<br>- ecologically relevant organisms (e.g. | Not accepted. Please refer to comment 174 above. |

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| | | | Amphipods from cold streams or stygophilous species like many copepods) under realistic low temperatures.<br>- Bacteria: Pseudomonas, Ames (TA 100 und 98), umu-Test<br>- Algae<br>- Makrophytes: *Myriophyllum aquaticum* (?)<br>- Fish: Fischeitest (DIN EN ISO 15088 – T6), Early-Life-Stage, Fisch-Embryo-Akut-Toxizität (acute fish-embryo toxicity; because these are the most vulnerable stages )<br>- Mouse-Lymphoma-test<br><br>Proposed change (if any): | |
| 176 | 238 | 6 | Comments:<br>Here, in chapter 5 of this draft, other ecotoxicological test should be named, in particular those, which are known to react sensitive to antibiotica and antiparasitica, e.g.:<br>- ecologically relevant organisms (e.g. Amphipods from cold streams or stygophilous species like many copepods) under realistic low temperatures.<br>- Bacteria: Pseudomonas, Ames (TA 100 und 98), umu-Test<br>- Algae | Not accepted. Please refer to comment 174 above. |

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| | | | - Makrophytes: *Myriophyllum aquaticum* (?)<br>- Fish: Fish egg- test, Early-Life-Stage, Fish embryo-Acute-Toxicicty (because these are the most vulnerable stages)<br>- Mouse-Lymphoma-test | |
| 177 | 238 | 11 | Comments: How to deal with multiple use substances (substances used as PPs, biocide, VMP and/or HMP) is mentioned in the background paragraphs (line 107-111). This should also be part of the actual guideline text (Chapter 5).<br><br>Proposed change:<br>Add text on how to deal with multiple use substances. Please take our general comment on this issue into account. | Not accepted. Please refer to the answer to comment 1 above. There is a comment from the same stakeholder on lines 248 about the same. Needs same answer as in here. |
| 178 | 239-263 | 9 | 5.1. Scenario 1: $PEC_{groundwater} \geq 0.1$ µg/l<br>5.1.1. Exposure assessment<br>5.1.2. Risk characterisation<br><br>Comments: Today, PEC ≥ 0.1 µg/l are regarded as unacceptable and a VMP with a PEC ≥ 0.1 µg/l does not comply with the criteria for authorization.<br>By introducing a new risk assessment approach as laid down in Scenario 1 for PEC ≥ 0.1 µg/l the draft calls for lowering the protection standards for human health and the ecosystem by accepting | Not accepted. The scenarios 1 and 2 explain the risk based approach for deriving PNEC values for the groundwater communities. This guideline has been drafted to move towards an environmental risk assessment based on a risk ratio approach (PEC/PNEC) for single active ingredients. |

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| | | | contaminations above 0,1 µg/l. This contradicts the precautionary principle that groundwater contamination is not acceptable.<br><br>Proposed change (if any): delete Point 5.1., 5.1.1. and 5.1.2. | |
| 179 | 239-274 | 4 | Comments: The difference between the approach developed in scenarios 1 and 2 is not obvious. In both scenarios, RQ groundwater is calculated using the same formula and should be >1. In addition, this is not clear why PEC and PNEC groundwater could only be refined in scenario 1 with PEC groundwater > 0.1 µg/l.<br><br>Proposed change: to clarify please rewrite chapter 5 with a single scenario whatever the threshold. | Not accepted. The need for an ERA for groundwater differs depending on the scenario (and threshold used). |
| 180 | 241-246 | 14 | Comments: I'm sorry but I disagree a bit with this point. I cannot see the reason why the Tier B should follow a protocol assessed for VMPs affecting manure communities. As suggested in the Lines 257-258, the $PNEC_{groundwater}$ can be refined, using the standard Tier B surface water tests (but still including the additional assessment factor of 10). | Noted. The text in this paragraph has been redrafted for clarity. |
| 181 | 242 | 14 | Comments: CVMP TGD (2016) is not quoted in the | Accepted. |

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| | | | Reference paragraph. It should be included in the list. | |
| 182 | 242-243 | 11 | Comments: it reads that the exposure can be refined. This is erroneous. The exposure *assessment* can be refined, which results in a more realistic predicted environmental concentration (PEC).<br><br>Proposed change:<br>Add assessment: If the initial concentration exceeds the GQS of 0.1 µg/l, the exposure assessment (PEC) can be refined. | Accepted |
| 183 | 243 | 4 | Comments: The $PEC_{groundwater}$ is first refined using the Focus Pearl Model and not $PEC_{surfacewater}$<br><br>Proposed change: Replace $PEC_{surfacewater}$ by $PEC_{groundwater}$ | Accepted |
| 184 | 243 | 4 | Comments: Focus Pearl Model will not be the first option for refinement but metabolism and manure degradation would be.<br><br>Proposed change: Line 244-246 please reword according to GL38 | Accepted |
| 185 | 243 | 11 | Comment: it reads $PEC_{surface\ water}$. This is an error | Accepted |

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| | | | and should be $PEC_{groundwater}$<br><br>Proposed change:<br>replace $PEC_{surface\ water}$ with $PEC_{groundwater}$ | |
| 186 | 243 | 11 | Comment 1:<br>Following CVMP technical guidance (and in VMP ERA practice), the PEARL CVMP-metamodel is used first (pages 46-49 of EMA/CVMP/ERA/418282/2005-Rev.1- Corr). Only if this model indicates a risk of leaching to groundwater, a PEARL simulation is needed. The groundwater document should refer to and follow the methods of the CVMP TGD guidance.<br><br>Comment 2: it should be mentioned that the relevant FOCUS scenarios should be used.<br><br>Note: it is advised to evaluate the applicability of the current scenarios regarding the application methods of VMPs to soil, since still pesticide scenarios developed for spray applications are used by default. This is not an issue for the current guideline, but a general issue regarding the use of the FOCUS scenarios.<br><br>Proposed change: | Accepted, these sentences were added<br>$PEC_{groundwater}$ can be refined following CVMP TGD (2016). First, the PEARL CVMP-metamodel for leaching to groundwater is run; based on the outcome of the metamodel it is established whether a PEARL simulation is necessary. PEARL should be run using the relevant scenarios and the parameters outlined in Appendix I of the CVMP TGD. The exposure assessment can also potentially be refined by determining degradation in manure in accordance with the respective CVMP guideline (EMA, 2011) and/or by using data on metabolism in the target animal. However, in this case (according to Phase II assessment) the exposure is based on the total residue approach, which considers both the parent compound and metabolites. Indeed, excreted relevant metabolites (≥10% of the administered dose) should be added to the active substance to allow the $PEC_{groundwater}$ to be recalculated. The fate of chemicals in the environment is dependent on their chemical/physical properties and degradability. These properties will vary between the parent compound and the individual excreted |

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| | | | Replace line 243-246 with.<br>$PEC_{groundwater}$ can be refined following CVMP TGD (2016). First, the PEARL CVMP-metamodel for leaching to groundwater is run; based on the outcome of the metamodel it is established whether a PEARL simulation is necessary. PEARL should be run using the relevant scenarios and the parameters outlined in Appendix I of the CVMP TGD. The exposure assessment can also potentially be refined by determining degradation in manure in accordance with the respective CVMP guideline (EMA, 2011) and/or by using data on metabolism in the target animal.<br><br>Note: text on dealing with metabolites (see general comment) to be added by the drafters. | metabolites. Consequently, if the level of groundwater exposure is first refined using degradation in manure and further refined using PEARL model, then $PEC_{groundwater}$ should be calculated separately for the parent compound and metabolites and subsequently summed up before to be compared with $PNEC_{groundwater}$. |
| 187 | 245 | 11 | Comments: it reads that the exposure assessment can be refined by determining degradation in manure.<br>We would like to stress that this refinement is potentially possible, but that determination of degradation in manure will invoke formation of degradation products that may need to be taken into consideration in the assessment.<br><br>In addition, if degradation in manure is put | Accepted. |

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| | | | forward as refinement, data on metabolism in the target animal should be mentioned as refinement option as well. Metabolism may contribute to a lower PEC and hence a refined exposure assessment. CVMP technical guidance lays down how this refinement could –potentially- be addressed. Also here, metabolites should be taken into consideration in subsequent assessment.<br><br>In all potential degradation stages (target animal, manure storage, soil) metabolites (=degradation products) or transformation products can be formed. As their environmental fate properties differ, their behaviour in soil during leaching to groundwater will be markedly different from that of the parent. Often, these substances are more mobile and /or more persistent in soil and thus more likely to leach into groundwater systems. The risk assessment of these metabolites/degradation products for groundwater should be part of this guideline.<br><br>Proposed change:<br>Add 'potentially' : The exposure assessment can also **potentially** be refined by determining degradation in manure in accordance with the respective CVMP guideline (EMA, 2011). | |

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| | | | Add potentially be refinement by taking account of metabolism in target animals. | |
| 188 | 245-246 | 1 | Comments: What about the refinement of the exposure assessment based on metabolism, excretion pattern (for ecto and endo parasiticides) and the degradation in soil? For the degradation in soil, for longer degradation times, you need to take into account the time necessary for leaching into groundwater.<br><br>Proposed change (if any): | Not accepted.<br>PECs are refined in line with VICH guidelines |
| 189 | 247 | 11 | Comment: The reasoning to only perform a risk assessment if the $PEC_{groundwater}$ is lower than 0.1 µg/l combined with a lowest PNEC for surface water lower than 1 or, if $PEC_{groundwater}$ is above 0.1 µg/l, is understood. However, for practical reasons and to prevent long discussions with applicants, it may also be advised to follow the pragmatic approach of always performing an ecotoxicological risk assessment in Tier B. This assessment is merely a calculation and does not include performing additional tests.<br><br>Proposed change: to be decided by drafters. | Thank you for your comment. However, this proposal is outside the scope of this guideline. |

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| 190 | 248 | 15 | Comment: please avoid the term “safe concentration” in this context; it is inappropriate in the context of regulatory principles and approaches and is an incorrect term from an ecological point of view.<br><br>Proposed change (if any): “In Phase II of the ERA the predicted no effect concentration for surface water species (PNEC surfacewater) is determined based on …” | Accepted. |
| 191 | 248 and further | 11 | Comments: $PNEC_{surface\ water}$. See earlier comment on line 237. A $PNEC_{surface\ water}$ is not defined nor derived within the CVMP ERA framework. PNECs are derived for individual taxonomic groups. See VICH Phase II guideline.<br><br>Proposed change: See comment at line 237 | Please refer to the answer to comment 172 |
| 192 | 248-254 | 4 | Comments: see comment and proposed change on lines 230-233: the use of an additional safety factor is insufficiently justified.<br><br>Proposed change (if any): | Noted. Please refer to the answer to comment 1 above, regarding the choice of AFs. |
| 193 | 252 | 14 | Comments: I do agree with the assessment factor (10) that has been indicated in this line. We | Noted. |

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| | | | performed a comparative study with a groundwater (*Diacyclops begicus*) and a surface water (*Eucyclops serrulatus*) copepod species, closed related from a phylogenetic point of view (the two species belong to the same family), showing that the groundwater species was 2-4 folds more sensitive than its epigean relative. | |
| 194 | 256 | 14 | Comments: CVMP GL (EMA, 2005) is not quoted in the Reference paragraph. It should be included in the list. | Accepted. |
| 195 | 257 | 4 | Comments: It appears to be a refinement of the PEC surface water PNEC, based on additional species/tests which are not necessarily applicable to ground water organisms<br><br>Proposed change (if any): | Noted. Paragraph has been re-drafted for clarification. |
| 196 | 258 | 4 | Comments: “No further”: There was no initial refinement based on ecotoxicological testing for groundwater species - in fact none of the above is based on testing of groundwater species.<br><br>Proposed change (if any): | Accepted. The term further has been removed. |
| 197 | 258 | 4 | Comments: a scientifically justified tiered | Not acceptable, the information on the refinement of |

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| | | | approach would be to compare the acute $PNEC_{surface\ water}$ to the $PEC_{groundwater}$ and if refinement is necessary (after full PEC-refinement), provide a chronic $PNEC_{surface\ water}$ for comparison with the $PEC_{groundwater}$<br>Proposed change: please consider revising the approach.<br><br>Proposed change (if any): | PEC and PNEC values follows VICH guidelines. |
| 198 | 259 | 2 | "long term test"<br><br>Comments:<br><br>Proposed change (if any): Correct into "long term tests" | Accepted |
| 199 | 259 | 3 | "long term test"<br><br>Comments:<br><br>Proposed change (if any): Correct into "long term tests" | Accepted. |
| 200 | 259 | 6 | "long term test"<br><br>Comments: | Accepted. |

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| | | | Proposed change (if any): Correct into “long term tests” | |
| 201 | 259 | 8 | “long term test”<br><br>Comments:<br><br>Proposed change (if any): Correct into “long term tests” | Accepted. |
| 202 | 261 | 11 | Comments: ' when a risk to the groundwater is indicated'<br><br>Proposed change:<br>‘when a risk to the groundwater compartment is indicated’ or ‘when a risk for groundwater is indicated’ | Accepted |
| 203 | 263 | 2 | “…the risk for groundwater has to be addressed in the benefit risk assessment”<br><br>Comments: What does the “benefit risk assessment” mean? Is it a comparison and subsequent evaluation of the benefits, compared to the risks?<br><br>Proposed change (if any): This should be explained more precisely. | Not accepted. Benefit/risk assessment within the framework of risk assessments of VMPs are considered well established concepts in the veterinary legislation and outside the scope of this guideline. |

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| 204 | 263 | 3 | "…the risk for groundwater has to be addressed in the benefit risk assessment"<br><br>Comments: What does the "benefit risk assessment" mean? Is it a comparison and subsequent evaluation of the benefits, compared to the risks?<br><br>Proposed change (if any): This should be explained more precisely. | Thanks for your comment. Please see the answer to comment 203, above |
| 205 | 263 | 6 | "…the risk for groundwater has to be addressed in the benefit risk assessment"<br><br>Comments: What does the "benefit risk assessment" mean? Is it a comparison and subsequent evaluation of the benefits, compared to the risks?<br><br>Proposed change (if any): This should be explained more precisely. | Thanks for your comment. Please see the answer to comment 203, above |
| 206 | 263 | 8 | "…the risk for groundwater has to be addressed in the benefit risk assessment"<br><br>Comments: Is this a spelling error (… benefir of risk assessment)? Or what does the "benefit risk assessment" mean? (is it a comparison and subsequent evaluation of the benefits, compared | Thanks for your comment. Please see the answer to comment 203, above |

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| | | | to the risks?)<br><br>Proposed change (if any): This should be explained more precisely. | |
| 207 | 263 | 11 | Comments: benefit risk assessment.<br>Proposed change:<br><br>Benefit:risk assessment or benefit/risk assessment | Accepted. |
| 208 | 264 | 11 | Comments: use subscripts in parameter naming<br><br>Proposed change:<br>edit header using subscripts | Accepted. |
| 209 | 264-271 | 9 | 5.2. Scenario 2: PEC groundwater< 0.1 µg/ l and PNEC surfacewater ≤ 1 µg/l derived from Tier B surface water toxicity tests<br><br>Comments: We welcome that the draft does recognize that the former detection limit of 0.1 µg/l can no longer be regarded as a safe limit value if the PNEC is below 0.1 µg/l, that organisms can be at risk at concentrations below that value and that the assessment for such cases must be refined. We support the proposed | Not accepted. The effects of multiple stressors are noted, but given their assessment constraints within risk assessment frameworks, it is considered outside the scope of this guideline. |

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| | | | changes in the assessment for PEC groundwater <0.1 µg/l.<br>But cumulative and synergistic effects of multiple restudies are not addressed. This should be amended in the draft.<br>A total limit value of 0.5 µg/l for mixture exposure of groundwater by VMPs, including active substances, their relevant metabolites, degradation products and reaction products, as it exists already for pesticides and biocides (laid down in Groundwater Directive (GWD) 2006/118/EC, Annex I), should be implemented for veterinary pharmaceuticals. In addition, known cumulative and synergistic effects should be taken into consideration in the risk assessment under scenario 2.<br><br>Proposed change (if any):<br>"For most VMPs, the PEC groundwater will be ≤ 0.1 µg/l. In these situations, a risk assessment for this compartment will not be needed, unless Tier B ecotoxicity data show that the PNEC surfacewater is ≤ 1 g/l. In this situation, the PNEC groundwater would be ≤ 0.1 µg/l (i.e., PNEC groundwater = PNEC surfacewater /10), and a risk to the groundwater compartment for a compound with a concentration < 0.1 µg/l may | |

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| | | | not be excluded. In this case, PNEC groundwater needs to be compared to the PEC groundwater in order to determine if there is a possible risk to the groundwater compartment, even if the PEC groundwater is ≤ 0.1 µg/l. **The risk assessment for substances with PEC <0.1 µg/l has to consider cumulative and synergistic effects. The risks of predicted concentrations of multiple residues of veterinary pharmaceuticals in groundwater ≤ 0.5 µg/l should be addressed accordingly.**" | |
| 210 | 264-271 | 15 | It is supported that effects on the groundwater ecosystem also need to be considered at concentrations lower than 0.1 µg/l in case of a risk assessment approach. | Thanks you for your comment. |
| 211 | 266 | 3 | For most VMPs, the $PEC_{groundwater}$ will be ≤ 0.1 µg/l.<br><br>Comment: Is this a prediction? Otherwise indicate reference.<br><br>Proposed change (if any): | Accepted. The sentence has been rephrased as follow: In situations where the $PEC_{groundwater}$ of VMPs will be ≤ 0.1 µg/l, a risk assessment for this compartment will not be needed, unless Tier B ecotoxicity data has shown that the $PNEC_{surfacewater}$ is ≤ 1 µg/l. In these cases, the calculated $PNEC_{groundwater}$ would be ≤ 0.1 µg/l (i.e., $PNEC_{groundwater} = PNEC_{surfacewater}/10$). In this case, the threshold value of 0.1 µg/l might not be protective for groundwater species. Consequently, the $PEC_{groundwater}/PNEC_{groundwater}$ ratio should be compared |

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| | | | | in order to determine if there is a possible risk to the groundwater compartment. |
| 212 | 266-271 | 4 | Comments: the use of an additional safety factor has not been scientifically justified<br>Proposed change: Please provide scientific evidence supporting the use of an additional safety factor, certainly since it has been shown in the frame of the WFD and GWD that surface water PNECs are protective for groundwater species, or delete the requirement for the additional factor.<br><br>Proposed change (if any): | Not accepted. It is considered that the use of an additional assessment factor is well supported by Section 4.2.1, 4.2.2 and 4.2.3 |
| 213 | 267 | 1 | Comments: Typo, should it read Tier **A** ecotoxicity data?<br><br>Proposed change (if any): | Accepted. |
| 214 | 267 | 2 | "…unless Tier B ecotoxicity data show that the PNECsurfacewater is ≤ 1g/l"<br><br>Comments: There must be a mistake here. Do the authors mean 1µg/l? | Accepted. |

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| | | | Proposed change (if any): This should be checked. | |
| 215 | 267 | 2 | Comments: If the authors mean 1µg/l: I am not sure, that I understand the argumentation. Why is a "safety" assessment factor of 10 introduced in section 4.2.4, and then revoked here? In order for the assessment factor to have an influence, the sentence should be changed into "…unless Tier B ecotoxicity data show that the PNECsurfacewater is ≤ 0,1µg/l". That way, the PNECgroundwater will be ≤ 0,01µg/l. In my opinion, this corresponds better to the plead for addressing the uncertainties from extrapolation of data from surface water species, as well as the risks resulting from the high sensitivity of groundwater communities (and their low recovery potential) – as stated in sections 4.2.1-4.2.4.<br><br>Proposed change (if any): change into "…unless Tier B ecotoxicity data show that the PNECsurfacewater is ≤ 0,1µg/l" | Not accepted. However, the paragraph has been re-drafted for clarification, as follows:<br>In situations where the $PEC_{groundwater}$ of VMPs will be ≤ 0.1 µg/l, a risk assessment for this compartment will not be needed, unless Tier B ecotoxicity data has shown that the $PNEC_{surfacewater}$ is ≤ 1 µg/l. In these cases, the calculated $PNEC_{groundwater}$ would be ≤ 0.1 µg/l (i.e., $PNEC_{groundwater} = PNEC_{surfacewater}$ /10), and a risk to the groundwater compartment for a compound with a concentration ≤ 0.1 µg/l may not be excluded. Consequently, $PNEC_{groundwater}$ needs to be compared to the $PEC_{groundwater}$ in order to determine if there is a possible risk to the groundwater compartment, even if the PEC groundwater is ≤ 0.1 µg/l. |
| 216 | 267 | 3 | "…unless Tier B ecotoxicity data show that the $PNEC_{surfacewater}$ is ≤ 1g/l"<br><br>Comments: There must be a mistake here. Do the authors mean 1µg/l? | Accepted |

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| | | | Proposed change (if any): This should be checked. | |
| 217 | 267 | 3 | Comments: If the authors mean 1µg/l: I am not sure, that I understand the argumentation. Why is a "safety" assessment factor of 10 introduced in section 4.2.4, and then revoked here? In order for the assessment factor to have an influence, the sentence should be changed into "…unless Tier B ecotoxicity data show that the $PNEC_{surfacewater}$ is ≤ 0,1µg/l". That way, the $PNEC_{groundwater}$ will be ≤ 0,01µg/l. In my opinion, this corresponds better to the plead for addressing the uncertainties from extrapolation of data from surface water species, as well as the risks resulting from the high sensitivity of groundwater communities (and their low recovery potential) – as stated in sections 4.2.1-4.2.4.<br><br>Proposed change (if any): change into "…unless Tier B ecotoxicity data show that the $PNEC_{surfacewater}$ is ≤ 1µg/l"<br><br>For extrapolating $PNEC_{groundwater}$ from $PNEC_{surfacewater}$ a safety factor of 10 is suggested to account for the predicted higher sensitivity of groundwater taxa compared to surface water | Not accepted. Please refer to the answer to comment 215 above. |

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| | | | taxa. The uncertainty of this prediction as well as effects of mixture toxicity and multiple stressors should be accounted for by an additional safety factor of 10. | |
| 218 | 267 | 6 | "…unless Tier B ecotoxicity data show that the PNECsurfacewater is ≤ 1g/l"<br><br>Comments: There must be a mistake here. Do the authors mean 1µg/l?<br><br>Proposed change (if any): This should be checked. | Accepted |
| 219 | 267 | 6 | Comments: If the authors mean 1µg/l: I am not sure, that I understand the argumentation. Why is a "safety" assessment factor of 10 introduced in section 4.2.4, and then revoked here? In order for the assessment factor to have an influence, the sentence should be changed into "…unless Tier B ecotoxicity data show that the PNECsurfacewater is ≤ 0,1µg/l". That way, the PNECgroundwater will be ≤ 0,01µg/l. In my opinion, this corresponds better to the plead for addressing the uncertainties from extrapolation of data from surface water species, as well as the risks resulting from the high sensitivity of groundwater communities (and their low recovery potential) – as stated in sections 4.2.1-4.2.4. | Not accepted. Please refer to answer to comment 215 above |

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| | | | Proposed change (if any): change into "…unless Tier B ecotoxicity data show that the PNECsurfacewater is ≤ 0,1µg/l" | |
| 220 | 267 | 8 | "…unless Tier B ecotoxicity data show that the $PNEC_{surfacewater}$ is ≤ 1g/l"<br><br>Comments: There must be a mistake here. Do the authors mean 1µg/l?<br><br>Proposed change (if any): This should be checked! | Accepted |
| 221 | 267 | 8 | Comments: If the authors mean 1µg/l: we are not sure, that we understand the argumentation. Why is a "safety" assessment factor of 10 introduced in section 4.2.4, and then revoked here? In order for the assessment factor to have an influence, the sentence should be changed into "…unless Tier B ecotoxicity data show that the $PNEC_{surfacewater}$ is ≤ 0,1µg/l". That way, the $PNEC_{groundwater}$ will be ≤ 0,01µg/l. In our opinion, this corresponds better to the plead for addressing the uncertainties from extrapolation of data from surface water species, as well as the risks resulting from the high sensitivity of groundwater communities (and their low recovery potential) – as stated in sections 4.2.1-4.2.4. | Not accepted. Please refer to answer to comment 215 above |

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| | | | Proposed change (if any): change into "…unless Tier B ecotoxicity data show that the $PNEC_{surfacewater}$ is ≤ 0,1µg/l" | |
| 222 | 267 | 11 | Comments: at the end of the line, it reads g/L<br><br>Proposed change: µg/l | Accepted |
| 223 | 267 | 15 | Comment: please change "is ≤ 1 g/l" to "is ≤ 1 µg/l" | Accepted |
| 224 | 272 | 11 | Comments: ' when a risk to the groundwater is indicated'<br><br>Proposed change: please adapt this wording (see line 261) | Accepted |
| 225 | 272-274 | 9 | "When a risk to the groundwater is indicated, the applicant should propose adequate risk mitigation measures to protect groundwater ecosystems. If no suitable risk mitigation measure/s can be applied, the risk for groundwater has to be addressed in the benefit risk assessment."<br><br>Comments: The assessment does not examine, if there are VMPs with the same mode of action or | Noted. Comparative assessments are not considered within the framework for veterinary medicines, and thus this suggestion is considered outside the scope of this guideline. |

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| | | | preventive measures that have less negative impact on the groundwater. To fill this gap, a comparative assessment, as it is already introduced in pesticide and biocide regulation, should be introduced. For further information see Regulation (EC) No 1107/2009.<br><br>Proposed change (if any): “When a risk to the groundwater is indicated, the applicant should propose adequate risk mitigation measures to protect groundwater ecosystems. If no suitable risk mitigation measure/s can be applied, the risk for groundwater has to be addressed in the benefit risk assessment~~.~~**, including a comparative assessment. If another authorised VMP already exists which presents a significantly lower overall risk for the groundwater, which is sufficiently effective and presents no other significant economic or practical disadvantages, an authorization shall not be granted.”** | |
| 226 | 279-282 | 4 | Comments: this reference can’t be accessed.<br><br>Proposed change: please provide a link for accessing the thesis | Noted. |

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| 227 | 321-322 | 4 | Comments: The link takes you to a page with an error 404: sorry, this page doesn't exist. The report referenced in the draft GL cannot be found anywhere on the UKTAG website.<br><br>Proposed change: please insert the correct link. | Noted |
| 228 | 321-322 | 15 | Comment: the link does not work; please check. | Noted |