20 November 2023
EMA/CVMP/ERA/156388/2023
Committee for Veterinary Medicinal Products (CVMP)

Overview of comments received on the 'Reflection paper on the environmental risk assessment of ectoparasiticidal veterinary medicinal products used in cats and dogs' (EMA/CVMP/ERA/31905/2021)

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

Stakeholder no.	Name of organisation or individual
1	The Swedish Society for Nature Conservation (SSNC)
2	Austrian Agency for Health and Food Safety, Institute for Plant Protection Products
3	Swissmedic (Swiss Agency for Therapeutic Products)
4	Federation of Veterinarians of Europe (FVE)
5	Access Vetmed
6	Andrea Tarr. Director, Veterinary Prescriber, veterinaryprescriber.org
7	Vet Sustain
8	German Environment Agency (UBA), section IV.1.2 - Biocides and IV2.2 - Pharmaceuticals
9	Buglife – The Invertebrate Conservation Trust
10	AnimalhealthEurope

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1. General comments – overview

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1	SSNC disagrees with the general assumption in Phase I ERAs (VICH GL 6) that VMPs intended for cats and dogs has a neglectable environmental exposure. Instead, SSNC considers that the environmental risk has been underestimated and that the presumption should be that these VMPs can harm the environment. Therefore, all VMPs intended for non-food-producing animals should progress to phase II ERAs so that information on fate, behaviour and effects are collected and evaluated. Also previously approved ectoparasiticidal VMPs should be evaluated in a phase II ERA. This is important to be able to compare environmental effect of all ectoparasiticidal VMPs, which is needed when choosing which treatments to be used within EU.	Thank you for your comments, which are acknowledged.
1	Several of the "major use" ectoparasiticidal VMPs can also be classified as PFAS according to the definition of OECD. This applies to fipronil, pyriprole, indoxacarb, lufenuron, afoxolaner, esafoxolaner, fluralaner, sarolaner, lotilaner and tigolaner. SSNC suggests a new section to be added in the reflection paper discussing this information, i.e. that several of the commonly used ectoparasiticidal VMPs are by definition PFASs, hence likely to be very persistent in the environment. This information should be considered in the environmental risk assessments.	Accepted. Thank you for your comment. Additional sentences have been added in sections 3.3, 5 and 6.1.1 accordingly. Please note that indoxacarb has not been highlighted as it belongs to a PFAS subgroup with key structural elements that have been shown to fully degrade under environmental conditions, according to the Annex XV restriction report.
1	SSNC agrees that risk mitigation measures (RMMs) can be one way to mitigate the exposure of active substance in the environment, and therefore urges that it should be mandatory provide RRMs	Thank you for your comments, which are acknowledged.

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	together with all approved ectoparasiticidal VMPs. However, some RRMs are today questionable, e.g. that animals to which spot on products have been applied should avoid to enter surface water for only 48h, although the product is working (i.e. being toxic to organisms) for 4 weeks. In addition, people (and treated animals) do not always follow the recommendations: Animals swim without permission, people do not bother/forget to remove collars etc. This potential lack of compliance should be considered in the ERAs. Moreover, SSNC requests that the product information should also include RMM for human exposure. Since many of these substances can harm human health contact with humans, primarily children, should be avoided.	Please note that the reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products (EMA/CVMP/ERAWP/409328/2010) is currently under revision and will address some of these points. Please also note that risks related to human exposure are addressed separately with a user safety assessment for every VMP, and are not within scope of this RP as explained in section 2.3.
1	SSNC encourage all ectoparasiticidal VMPs for pets to be classified as prescription-only medicines in all Member States. The environmental impact of these drugs is too severe for the drugs to be sold over the counter.	Thank you for your comment, which is acknowledged. Chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view.
2	We greatly appreciate the effort to shine some light onto the topic of environmental risk assessment of ectoparasiticidal VMPs. Based on the available information presented in this reflection paper regarding potential environmental exposure, and under consideration of the active substances used, we agree with the authors' conclusion that the negligibility of environmental exposure from the use of these	Thank you for your comment.

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	VMPs may be questioned. The presented information and literature show that the current approach of stopping the ERA in phase I should be reconsidered.	
3	Swissmedic welcomes the opportunity to comment on this well written and detailed reflection paper. The reflection paper focuses on considerations regarding the ectoparasiticidal drugs imidacloprid, fipronil and fluralaner and recommends that environmental monitoring of such parasiticides used in cats and dogs should be continued. However, imidacloprid has been used widely in horticulture and agriculture and, in the future, many legal and illegal uses outside of companion animal medicine are still to be expected. It is similarly likely that illicit uses of fipronil will occur in the future. Fluralaner is approved for use in poultry. Imidacloprid and fipronil are also approved in ferrets. Therefore, any environmental contamination of e.g. surface waters with these drugs may originate from uses other than their application as parasiticides in cats and dogs, thus limiting the interpretation and impact of future environmental monitoring studies. As a consequence, we believe that the reflection paper should explicitly recommend that future environmental monitoring plans must include one or more representatives of isoxazolines (in addition to fluralaner) that are used exclusively in cats and dogs across Europe.	Thank you for your comments. The EMA/CVMP fully agrees with Swissmedic that the multiple and often unverifiable use of active substances limits the interpretability of non-targeted monitoring studies. Chapters 6.3 and 7 have been revised.
3	Due to the low water solubility of isoxazolines, measurements should be carried out not only in water but also in sediments.	Thank you for the comments.

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	In general, systemic application of ectoparasiticidal VMPs results in large quantities (up to 80% of the compound in the case of isoxazolines) being excreted via fecal shedding, which then ends up in the terrestrial compartment, especially in areas with high density of dog/cat populations. The potential impact of excreted drug residues from treated animals on the terrestrial environment is not really looked at, although the authors indicate that there is a clear tendency of increasing use of systemic application of novel drugs such as isoxazolines or even combination products with macrocyclic lactones. Therefore, measurements of isoxazolines should also be carried out in soil, especially in highly used urban and peri-urban areas.	Please note that sediments are already addressed in the RP in the conclusions on fate and exposure data, in the discussion of possible monitoring options and in the general conclusions. Recommendations for measurements carried out in soil in highly frequented areas have been addressed more clearly now.
3	While drugs affecting neuronal targets are comprehensively mentioned in this reflection paper, there is little information on chitin synthase inhibitors such as lufenuron, which has been on the market as ingredient in oral suspensions, injections and tablets for cats and dogs for a long time. In this respect it is important to note that susceptible non-target organisms, such as insects and invertebrates that rely on chitin synthesis to complete development may suffer population declines, which may have a negative impact on ecosystems. Lufenuron is stored in fat tissue, remains there for several months, and is excreted via feces basically unchanged. A more recently paper discusses this aspect in detail: Schmid S, Song Y, Tollefsen KE. AOP Report: Inhibition of Chitin Synthase 1 Leading to Increased Mortality in Arthropods. Environ Toxicol Chem. 2021 Aug;40(8):2112-2120. doi: 10.1002/etc.5058. Epub 2021 Jun 30. PMID: 33818824.	Thank you for the comment. As kindly suggested, the mentioned research article has now been included in the Annex.

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3	Another aspect that could be mentioned is the fact that isozaxolines are also being investigated for their potential of application as transmission blocking agents to fight vector-borne diseases, notably affecting humans. For a range of drug classes commonly used in companion animals, namely avermectins, milbemycins, isoxazolines and spinosyns, simulations predicted that isoxazolines and spinosyns are promising candidates for mass drug administration, as they need less frequent application than avermectins and milbemycins to maintain mosquitocidal blood concentrations. (Meredith et al. Optimising systemic insecticide use to improve malaria control. BMJ Glob Health. 2019 Nov 11;4(6):e001776. doi: 10.1136/bmjgh-2019-001776. PMID: 31798988; PMCID: PMC6861066.). Another paper suggested that isoxazolines should be used in humans for the reduction of vector-borne disease incidence, more specifically Malaria (Miglianico et al. Repurposing isoxazoline veterinary drugs for control of vector-borne human diseases. Proc Natl Acad Sci U S A. 2018 Jul 17;115(29) E6920-E6926. doi: 10.1073/pnas.1801338115. Epub 2018 Jul 2. PMID: 29967151; PMCID: PMC6055183.) In addition, work is in progress to develop isoxazoline-based inhibitors which exhibit direct anti-protozoal activity, most notably against malaria and against leishmaniasis. (Galbiati A, Zana A, Coser C, Tamborini L, Basilico N, Parapini S, Taramelli D, Conti P. Development of Potent 3-Br-isoxazoline-Based Antimalarial and Antileishmanial Compounds. ACS Med Chem Lett. 2021 Oct	Thank you for the interesting references. Your comments are acknowledged. However, research on possible future uses of certain substances as human medicine is not in scope of this RP. Please note that this RP has been written considering the ERA for VMPs used in cats and dogs.

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	13;12(11):1726-1732. doi: 10.1021/acsmedchemlett.1c00354. PMID: 34795860; PMCID: PMC8591724). Overall widespread administration of these isoxazoline compounds in the human population will also contribute to increased environmental pressure, probably to a larger extent than the use as ectoparasiticidal VMPs, and this by itself is also a good argument to further proceed with environmental risk assessments of these compounds. A more recent paper has investigated the use of systemic parasiticides in livestock to control zoophilic malaria vectors contributing to residual malaria transmission, and authors propose to treat cattle with ivermectin, fipronil, and afoxolaner to significantly reduce the larval production of surviving Anopheles stephensi and A. albimanus, which transmit malaria. Implementation of this strategy to manage zoophilic vectors would also increase environmental risks (Dreyer et al. Survival and Fecundity of Anopheles stephensi and Anopheles albimanus Mosquitoes (Diptera: Culicidae) After Ingesting Bovine Blood Containing Various Veterinary Systemic Parasiticides. J Med Entomol. 2022 Sep 14;59(5):1700-1709. doi: 10.1093/jme/tjac103. PMID: 35934895; PMCID: PMC9473655).	
3	Some additional references could be added. For instance, a paper on the ecotoxicity prediction of pyrisoxazole transformation products formed in soil and water. Pyrisoxazole is a isoxazoline compound used as anti-fungizide d (Jiao B, Zhu Y, Xu J, Dong F, Wu X, Liu X, Zheng Y. Identification and ecotoxicity prediction of pyrisoxazole transformation products formed in soil and water using an effective	Thank you for the references. As kindly suggested, the review article on the toxicity fipronil degradation products has now been included in the Annex of RP.

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	HRMS workflow. J Hazard Mater. 2022 Feb 15;424(Pt A):127223. doi: 10.1016/j.jhazmat.2021.127223. Epub 2021 Sep 21. PMID: 34600378.) Or a comprehensive review on the environmental degradation of fipronil and its toxic metabolites (Singh NS, Sharma R, Singh SK, Singh DK. A comprehensive review of environmental fate and degradation of fipronil and its toxic metabolites. Environ Res. 2021 Aug;199:111316. doi: 10.1016/j.envres.2021.111316. Epub 2021 May 11. PMID: 33989624.	Pyrisoxazole is not in scope of this RP, as only ectoparasiticidal and endectocidal active substances contained in VMPs currently authorised through the central and/or national authorisation procedures in the EU/EEA are addressed.
4	FVE welcomes the CVMP intention to re-assess the ERA approach and supports the considered new ERA methodology whereby • the current approach to stop the ERA in "phase I" should be reconsidered; • assessment focus on environmental risks on surface waters (including sediments) for both systemically- and locally-acting VMPs; • risk mitigation measures may require re-evaluation to able to mitigate the exposure of the active substances in the environment • monitoring environmental concentrations should be considered as part. Nevertheless, FVE would like to highlight the need for careful assessment of the origin of such substances found in the	Thank your comments. The CVMP fully agrees with FVE.

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	environment. Substances might be used in other sectors as well, e.g. biocides, plant protection, etc. Without defined data sources, conclusions to the real contribution of the use as veterinary medicinal products (VMPs) authorized for use in companion animals might be misleading. As a result, risk management measures for those VMPs might be not meaningful in the end to control a certain observed environmental risk. Furthermore, environmental impact needs to be also weighed against approaches to control parasite infections and associated health risks for companion animals and consequently humans living with them. The availability of authorized treatment options for ectoparasitic diseases in dogs and cats should be ensured throughout Europe. FVE would like to reiterate the need for making those products POMs (prescription-only). Prescription of those products after consultation by a veterinarian can contribute to more responsible use of those products by avoiding blanket treatment and the easier monitoring of their use, allowing that way for a better insight into the actual use of those products (e.g. https://www.bva.co.uk/media/4715/bva-responsible-use-of-parasiticides-for-cats-and-dogs-the-5-point-plan.pdf).	Chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view.
5	Access VetMed welcomes the opportunity to comment on this draft reflection paper. The pragmatical and scientific approach to this potential environmental concern is appreciated. It is noted that, while there are certain indications that ectoparasiticidal VMPs for cats and dogs could lead to environmental	Thank you for your comments. CVMP agrees that further monitoring data are necessary, however, please note that the main aim of closing data and knowledge gaps is not to better understand the contribution of VMPs to environmental concentrations compared to other (e.g. biocidal or pesticidal) sources. Instead, such data are necessary to get a better

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	concentrations of these active substances, it is not possible to quantify the contribution of parasiticidal VMPs for cats and dogs to the environmental concentrations in wastewater and surface waters. It is likely that the most relevant sources of these substances in the environment are PPTs and biocides. Therefore, further monitoring would be necessary before establishing conclusions concerning the environmental risks of ectoparasiticidal VMPs for cats and dogs.	understanding of the specific environmental exposure pathways and fate of these substances to subsequently allow for a quantitative risk assessment for specific VMPs and product types to allow for adequate recommendations and specific, product-based RMMs. As outlined in the discussion of the RP, future ad-hoc monitoring studies carried out at potential hotspots will be more suitable to give better understanding on the emissions from the use of ectoparasiticidal VMPs compared to currently available monitoring data. Chapters 6.3 and 7 have been revised.
6	Thank you for the opportunity to comment on this paper. I broadly agree with the contents of the paper and with the proposals: to fill knowledge gaps about parasiticide drugs used in companion animals; revisit the current approach of stopping environmental risk assessment in phase I; monitoring environmental concentrations in the environment; regulating the sale of parasiticides/consideration of environmental safety when assigning prescription status; raising awareness on the environmental hazards of these products; promoting the prudent use of veterinary medicines; promotion non-medical preventive measures; improving product literature. I have specific comments on the following areas: **Endectocides as wormers** The focus of the reflection paper is on the use of ectoparasiticides and endectocides in the control of ectoparasites. The paper recognises (line 304 onwards) that ectoparasiticide drugs are	Thank you for your comments. Your comments and concerns regarding the endectocides are acknowledged. Please note that, in a first pragmatic step, it was necessary to limit the scope of this RP to bring the topic forward and to achieve the objectives defined (see chapter 2.3 for

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	included in combination products that are also indicated for the control of worms, and also that endectocides have a dual effect (including potentially on organisms in the environment). However, I believe that more attention needs to be given to the role of endectocides in contributing to environmental pollution. Only one endectocide drug is included in products for its ectoparasite effects (selamectin); most of the endectocides in authorised parasiticides are used for their worming effects (eprinomectin, milbemycin, moxidectin). If these end up in the environment and persist they will potentially adversely affect non-target organisms. Therefore it is also important to consider the factors that drive the use of wormers and combination products. These include: • Exaggeration of the benefit to human health of worming pet dogs and cats to control Toxocara. (Patterson J Toxocarosis in humans: how much of a problem is it in the UK? Drug and Therapeutics Bulletin 2023;61:7-11; Tarr A Toxocarosis: a One Health issue Drug and Therapeutics Bulletin 2023;61:3. • Subscription schemes promoted through veterinary practices in the form of Pet Health Plans • Prevention of Angiostrongylus vasorum, which drives monthly prescription of endectocides (the only wormers authorised to prevent A. vasorum). There is a need for more evidence about the burden of A.vasorum disease in dogs from(including mortality), about whether less frequent than monthly treatment prevents disease, and about the role of test and treat in maintaining the health of dogs.	details) rather than addressing the wide-ranging topic of ERA for all parasiticidal VMPs for companion animals. Therefore, the environmental risks of substances used in VMPs for their endoparasiticidal activity are not within the scope of this RP, albeit CVMP acknowledges that is not possible to draw a clear line between those substances and ectoparasiticides.

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	Regulation of sales In the UK there has been a growth in the availability of parasiticide subscription schemes • Through veterinary practices (as part of pet health schemes) • Directly to pet owners (some of which offer incentives to subscribe – free toys or treats). • It is inappropriate for medicines of any kind to be available on subscription/box-schemes. • There has been deregulation in the UK so that many parasiticide products are now available to purchase without any professional advice (i.e. on general sales). Given the recognition of the harmful effects on the environment, it can be argued that there is a need for re-evaluation of the supply classification of parasiticides, so that they are only available with professional advice to ensure their appropriate use (perhaps with a requirement for a written justification for their prescription) and on safe handling.	Please note that the regulation of prescription status or sales in the UK are not within the remit of EMA/CVMP. Chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view.
	Product literature There is a need for clearer information for parasiticide users in the package information. Typically, a package leaflet for a veterinary medicine contains a lot of detail in highly technical language, is not set out in a way that is most helpful to lay readers, and important information about safe use is hidden deep within the leaflet, where it may not be seen. With respect to collars in particular, the	Your comments are acknowledged. Please note that for the EU/EEA the reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products (EMA/CVMP/ERAWP/409328/2010) is currently under revision and will address some of these points.

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	information about potential effects on the environment is unclear and seems inconsistent between products (see below): • **Beaphar flea and tick collar for dogs** (active ingredient: dimpylate; lasts 4 months; on general sales)**:** **"**BEAPHAR FLEA & TICK COLLAR FOR DOGS is a water-resistant collar" **"**This collar is EXTREMELY DANGEROUS to fish and aquatic life. Do not contaminate ponds, waterways or ditches with the collar or empty packaging." *What does water-resistant mean? Does it mean your dog should not swim – with or without the collar?* • **Scalibor, Canishield** (deltamethrin; lasts 5 to 6 months; NFA-VPS) **Scalibor**: "While occasional contact with water does not reduce the effectiveness of the collar, it should be removed before swimming and bathing the dog because the active substance is harmful to fish and other aquatic organisms. Dogs must be prevented from swimming in water for the first five days of wearing the collar". "Dispose of waste material in accordance with local requirements. Scalibor should not enter water courses as this may be dangerous for fish and other aquatic organisms." **Canishield**: "Deltamethrin is continuously released from the collar to the skin and fur whilst the collar is being worn". "Deltamethrin is toxic	Product specific requirements will need to be discussed on a case-by-case basis. However, general changes to the requirements for product literature are outside the scope of this RP.

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	for aquatic organisms. Dogs wearing the collar are not allowed to enter watercourses." Different information for similar products. **Seresto** (imidacloprid, flumethrin; lasts 8 months; POM-V): "Water-resistant product". The collar should be worn continuously for the 8 month protection period" "The product is water resistant; it remains effective if the animal becomes wet. However, prolonged, intense exposure to water or extensive shampooing should be avoided as the duration of activity may be reduced." "Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. This product should not enter water courses as it may be dangerous for fish and other aquatic organisms." *No message about not letting your dog swim.It can be read as though it is safe for dog to swim in the collar.*	
7	Vet Sustain is supportive of the proposal by CVMD to reassess the ERA approach whereby: • the current approach to stop the ERA in "phase I" should be reconsidered. • assessment focus on environmental risks on surface waters (including sediments) for both systemically- and locally acting VMPs; • risk mitigation measures may require re-evaluation to able to mitigate the exposure of the active substances in the environment.	Thank you for your comments.

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	• monitoring environmental concentrations should be considered as part. We also consider that routes of supply are an important part of environmental risk, whereby parasiticides with a potential risk to the environment should only be available through certified, trained sources such as a vet or SQP. In this way, an appropriate balance of need and risk can be assessed and recorded, accompanied by appropriate tailored advice to meet the needs of both animal welfare and the environment.	Chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view.
8	The Chemical Safety Department of the German Environment Agency appreciates the reflection paper and its conclusions. It is of high importance to investigate the emission of products used in companion animals into the environment and to later develop a targeted environmental risk assessment of relevant product groups. In the context of the upcoming one substance one assessment concept, the potential re-use of data already available for substances also in current or past use in other frameworks such as biocides, pesticides or human medicines could be considered.	Thank you for your comments. Indeed, for many of the active substances within the scope of this reflection paper, comprehensive data sets on environmental hazard assessments and effects data from ERAs conducted under other legislative frameworks are available and could be used for ERAs of the ectoparasiticidal VMPs, which is mentioned at the beginning of chapter 5 and also later in the RP at several instances. Chapter 6.4 has been updated accordingly.
9	This reflection paper provides a good overview of the issues surrounding ectoparasiticidal substances impact on the environment. However, many actions to reduce the impact on the environment, particularly the freshwater environment have been missed. Buglife's 2017 report: *Neonicotinoid Insecticides in British Freshwaters* should be referenced, and recommendations adopted where applicable to relevant ectoparasiticidal substances. Further	Thank you for highlighting this reference. Please note that the imidacloprid concentrations in British freshwaters are addressed in other peer-reviewed papers referenced in the RP.

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	to this, the comments below specify some areas that should be improved.	
9	We would like to see the correct application of the precautionary principle with regards to Veterinary Medicines. Given the known impacts and pathways of chemicals such as fipronil and imidacloprid, as well as their ban in agricultural use, greater urgency is required to prevent any risk to the environment.	Thank you for your comment, which is acknowledged. Please note that the precautionary principle is currently applied with the *product-class* based, general precautionary risk mitigation measures (RMM) for spot-ons and collars, due to the absence of individual *product-specific* ERAs. The recommendations for such RMM are currently being updated. For individual products the precautionary principle could only be applied as part of the benefit-risk assessment with a *product-specific* ERA in place.
9	The recommendations in this reflection paper do not go far enough to protect the environment given existing knowledge about the effects of fipronil and imidacloprid. Greater evidence of the effectiveness awareness of is required before awareness is recommended as primary approach. Instead, alternate actions such as making these medicines prescription only will reduce routine use and misuse.	Thank you for your comment. Chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view.
9	The use of Imidacloprid as an externally applied veterinary medicine should be suspended this is the measure most likely to rapidly reduce chronic pollution levels.	Thank you for your comment. Please note, that the authorisation of a VMP is always based on a positive overall benefit-risk balance, which does not only consider risks such as to the (target) animal, the user and the environment, but also the direct therapeutic and indirect or additional benefits.

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		Please also note – as highlighted in the RP – that the environmental exposure pathways of the specific formulations and substances (also beyond imidacloprid) are not yet fully understood and the source apportionment of measured concentrations is mostly not possible.
9	A further recommendation should be to include additional chemicals use in ectoparasiticidal substances onto watchlists. Monitoring of the substances discussed in this reflection paper should be pursued, regardless. of their future Watch List status. This should be a clearer recommendation of this paper and applied to address data gaps.	Thank you for your comment, which is acknowledged. Please note that the recommendations on monitoring options in the RP have been revised in chapters 6.3 and 7.
9	Surveillance data must be gathered and published routinely to ensure the best actions are taken to protect the environment. The best measure to gather data on usage of ectoparasiticidal VMPs would be to make them prescription only. Not only would this improve monitoring of sales, but it would also provide increased awareness of correct application and impact.	Thank you for your comment, which is acknowledged. Please note that the establishment of a surveillance system on the sale and use for such products is legally not foreseen and outside of the remit of the EMA/CVMP. However, as explained in chapter 4.1, aggregated data on the volumes of sales should become increasingly available to national competent authorities (NCAs) in the future. As mentioned above chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view.
10	AnimalhealthEurope welcomes the opportunity to comment on this timely reflection paper. We agree that further research is needed to investigate potential environmental emissions of ectoparasiticides	Thank you for your comments.

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	for cats and dogs when used according to the registered labels. However, proper assessment of other potential sources of emission such as biocidal uses should be considered too. The overall thrust of the reflection paper is that a lot of studies are highlighted, but with minimal commentary on findings. Many assumptions are made, but overall, it highlights significant lack of evidence.	Please note that the main aim of closing data and knowledge gaps is not to compare the contribution to environmental concentrations of VMPs with those of other (e.g. biocidal or pesticidal) sources. Instead, such data are necessary to get a better understanding of the specific environmental exposure pathways and fate of these substances, to subsequently allow for a quantitative risk assessment for specific VMPs and product types, and to allow for adequate recommendations and specific, product-based RMMs. As outlined in the discussion of the RP, ad-hoc monitoring studies carried out at potential hotspots for substances that are exclusively used in cats and dogs will be more suitable to give a better understanding on the emissions from the use of ectoparasiticidal VMPs than currently available monitoring data. Please also note that the present RP has been written from the perspective of the VMP framework and it addresses the issues related to this framework. A proper assessment of emissions covered by other frameworks is not the within the scope of this document and outside of the remit of the CVMP. As outlined throughout the RP, there may be lack of evidence for the level of contribution of these VMPs to environmental concentrations of certain active substances. However, there is no lack of evidence on their parasiticidal activity or their global market share or widespread use. In

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		view of the apparent concerns and taking into account the precautionary principle, all potentially harmful effects of a product should be identified and a scientific risk assessment should be sought.
10	Whilst spot-on's are predominantly mentioned there is lack of differentiation of systemic or topically acting products which is a deficiency. Particularly as the distribution and elimination and potential for environmental contamination are so different between the products with these different modes of action.	Not agreed. Please note, that monitoring data and proposed exposure models are currently only available for topically-acting substances. Therefore, no differentiation was necessary in the respective chapters. In all other parts of the RP, a differentiation based on mode of action (systemically- or locally-acting) and route of application (systemic or topical administration) has been made, where relevant.
10	A number of references cited in the RP take the form of letters to the Vet Record *e.g.*, Little et al (Line 100). Such letters merely state the authors opinions, and have not been subject to peer review. The RP evidence should be based on peer reviewed scientific research and scientific data (assessed in the context of a regulatory procedure) for which an opinion has been published. We propose that references to such letters are removed from the RP.	Partially agreed. The purpose of this RP is (amongst others) to communicate the CVMP's view on the current state of the scientific discussion. These letters referenced in the RP give an overview of the ongoing scientific discussion, their citation is therefore considered justified. The last sentence of the paragraph explains that data situation calls for a more in-depth evaluation. That being said, a more precise text has been added for more clarity.

Stakeholder no. *(See cover page)*	General comment (if any)	Outcome (if applicable)
10	As the authors themselves state throughout the document, both data sources as well as exposure model are not suitable for a reliable ERA of VMPs. Emission data was only estimated based on unreliable and incomplete data sources such as pet population and sales data. In addition, monitoring data of selected APIs in the case studies of the RP are not suitable data sources as well, as distinction between emissions from VMP, PPP, or biocides is not possible (lines 800) both in agricultural (1127-1133) as well as urban areas (1134-1142). *E.g.*, the use of imidacloprid as a biocide has been recently extended by the European Commission until 31 December 2025 (COM Implementing Decision (EU) 2023/460) Exposure models that were used are also described as not appropriate (line 772). In the absence of reliable input data and exposure models any conclusion from the case studies and any assessment of a potential risk are of limited value and any additional RMMs based on the findings are hardly justified – which is again acknowledged by the authors themselves (1430-1433). While industry agree that a reasonable path forward would be to close data and knowledge gaps and continue monitoring to better understand the contribution of VMPs, we think other proposed measures like emphasizing environmental hazards of products without being able to assess the associated risk might be inadequate and would rather be harmful by undermining the pet owner´s trust in these VMPs in general.	Not agreed. The main aim of closing data and knowledge gaps is <u>not</u> to compare the contribution to environmental concentrations of VMPs with those of other (e.g. biocidal or pesticidal) sources, but to get a better understanding of the specific environmental exposure pathways and fate, and subsequently on the risks of specific VMPs and product types, and to allow for adequate recommendations and specific product-based RMMs. This includes the development or improvement of suitable exposure models for such VMPs. The sustainable and prudent use of pharmaceuticals, however, should always be encouraged considering a 'One Health' approach. Public awareness and public education are key elements in such efforts, which includes being transparent to pet owners (and veterinarians) on known environmental properties/hazards of active substances used. This is considered beneficial for the promotion of a responsible use.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
57	10	**Comment:** Neglected overstates the case, in recent years more work has been done **Proposed change:** please change "neglected" to "limited"	Partly accepted. Considering the extent of the data gaps identified in the present RP, the wording hast been changed to 'very limited'.
62	10	**Comment:** Typo **Proposed change:** "Guideline**s**"	Not accepted. The sentence lists a series of guidelines: "(VICH) guideline (GL) 6 (EMA, 2000) **and** VICH GL 38" Therefore, no changes to the reflection paper are considered necessary.
76–81	10	**Comment:** The reference to the "actual dose" is misleading as the dose is irrelevant for currently implemented rules to stop an ERA for companion animals in Phase I, it is the lower number of animals being treated. Moreover (L78) the dose applied to the animal cannot be considered equal with the environmental exposure. There are many different exposure scenarios, each one associated with potential depletion of the API through absorption, degradation, metabolism, etc. Additionally, some may need or have a phase II ERA. **Proposed change:** Consequently, to this day, **most** VMPs intended for use in cats and dogs and other non-food-producing animals usually do not require the performance of a phase II ERA~~, regardless of the actual dose applied to the animals (i.e. environmental~~	Partly accepted. The wording has been slightly revised.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		~~exposure),~~ such that about two thirds of all products authorised until 2020 did not progress to a phase II ERA solely because of the fact that they were intended for use in companion animals (Fabrega and Carapeto, 2020).	
104–106	10	**Comment:** The statement that a potential link between the death of songbird chicks and the treatment of dogs with parasiticidal VMPs was highlighted in Guldemond et al. (2019) is not correct and needs to be deleted. In fact, Guldemond et al. (2019) conclude that the pesticides detected in the dead chicks are most probably not the cause of death (with active substances used in VMPs being covered by the term "pesticide"). Guldemond et al. (2019) demonstrate however a potential transfer of active substances from hair of treated dogs to the chicks. **Proposed change:** In addition, a potential **transfer of parasiticidal VMPs** ~~link between the death of~~ **from the hairs of treated dogs to** songbird chicks ~~and the treatment of dogs with parasiticidal VMPs~~ was highlighted in another recent publication (Guldemond *et al.*, 2019).	Not accepted. Guldemond et al. (2019) state "[…] However, veterinary products fipronil and imidacloprid, which are highly toxic to birds, could be the cause of the death of young great tits in two cases due to the high concentrations found". Therefore, no changes to the RP are considered necessary.
135	10	**Comment:** Given the fact that exposure pathways will also include surface water environments, the limitation to non-target insects and mites is inappropriate. **Proposed change:** Ectoparasiticidal VMPs intended for use in cats and dogs have an insecticidal and	Accepted. The RP has been amended accordingly.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		acaricidal activity that could impact free-living non-target insects and mites **and other arthropods** and thus impact ecosystems.	
159, Table 1	10	**Comment:** It is stated in table 1 that the RP does not consider companion animals other than cats and dogs. According to FEDIAF (2020), there are about 18 million small animals in the EU/EEA, and some parasiticides are approved for the use in *e.g.*, rabbits or ferrets. Will small animals be considered as "minor species" as an exposure to the environment is unlikely due to their rearing conditions? **Proposed change:** Please add a reference	Not accepted. The scope of the RP was limited considering a pragmatic approach in order to achieve the defined objectives as explained in the paragraph above. General conclusions are transferable to other companion animal species, specific conclusions, e.g. on environmental exposure pathways, need to be considered separately. Therefore, no additional reference is deemed necessary.
168–172	10	**Comment:** The same is true for pet population as a measure of environmental emission.	Comment acknowledged, albeit no changes to the sentence are deemed necessary.
182–183	10	**Comment:** For the estimation of the emission of parasiticides for companion animals to the STP, a default value for the number of animals per STP would be needed. However, the development of an average default for an assessment on EU/EEA level would lead to great over- or underestimations, as there is a large range on country-level. According to FEDIAF (2020), which is cited in this RP, in Greece, only 14% of the households own a dog or a cat, respectively, whereas 42% of the households in Poland and Romania own a dog or a cat, respectively. **Proposed change:** Please use country specific considerations instead of an EU default.	Not accepted. Please note that this paragraph describes the cat and dog population in Europe. No default values for emission estimates from STP are defined or suggested in this section or later in the document. Please also note that text in the following line states that there are large differences between countries. Therefore, no changes to the RP are deemed necessary. That being said, it is acknowledged that this may be an interesting point for future exposure model developments.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
205–209	10	**Comment:** 2012/2013 publications are cited to underline continued use of older APIs. To be able to make such assumptions, current data is needed, as practices might have changed. **Proposed changes:** Please update the references with new and recent data.	Not accepted. Please note that this is a chronological outline of the developments. More recent references are given in the following lines. Please also note that no quantitative information on current use practices are given. Therefore, no changes to the text are deemed necessary.
342–343	10	**Comment:** Publication of Zhou et al, 2021 is a review article. **Proposed change:** Please cite original source publications to support CVMP's statement that feeding conditions influence bioavailability.	Not accepted. Please note that review papers have been cited, as they combine the results of multiple papers. This is considered a more efficient way to cover many years of research.
354–359	10	**Comment:** Speculative wording with no evidence within text. **Proposed change:** Please remove the paragraph or substantiate with data.	Partly accepted. These are not speculative sentences. Please note that the (legal) distribution channels in the Member States are known by the Competent Authorities. Please also note that Competent Authorities deal with any illegalities (intentional and unintentional violations of the legislation) related to distribution channels on the medicinal market. That being said, the wording has been slightly amended for more clarity.
356–358	10	**Comment:** How can illegal sales be the responsibility of the MAH? **Proposed change:** Please remove the reference to illegal sale.	Not accepted. No responsibility of the MAHs regarding illegal sales is stated in the text whatsoever. Please also refer to the response to the previous comment.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
			Please note this section aims to describe and understand the current situation in Europe and that in order to do so all possibilities and responsibilities need to be considered.
391 Table 4	8	**Comment**: We recommend to enlarge the table for the approval status of active substances with ectoparasiticidal and endectocidal activity be marketed in human medicinal products (HMP). At least in Germany numerous HMPs are currently marketed with the following active substances: permethrin, piperonyl butoxide, ivermectin. This emission source, which has not yet been considered, might be relevant for the interpretation of positive detections in environmental samples. **Proposed change**: Additional column: Human medicinal products approval status Permethrin → Marketed Piperonyl butoxide – Marketed Ivermectin – Marketed	Partly accepted. Thank you for your comment. As HMPs are not within the scope of this RP, the respective authorisations have not been assessed in the initial survey conducted among the Member States and, therefore, no comprehensive data are available to be included in this RP. The CVMP agrees that emissions from use in HMPs might be relevant for the interpretation of environmental concentrations of some active substances, albeit, this is, to the best of our knowledge, not the case for the exemplary substances mainly discussed in this RP (imidacloprid, fipronil, fluralaner). Please also note that it is outside the remit of the CVMP to confirm or refute the contribution of PPPs, biocides or other products to environmental concentrations of active substances. That being said, the paragraphs on permethrin and piperonyl butoxide in the annex of the RP have been amended to also account for HMPs. No changes to the table are deemed necessary or possible at this point.
391 Table 4	8	**Comment:** For the substance Fenoxycarb the Biocide Approval status should be adapted as the approval for the use as biocidal active substance in product type 8 has expired.	Accepted. Thank you for the comment. The table has been updated accordingly.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change: Biocide Approval status → expired	
391 and ff Table 4	10	**Comment:** While the use of certain active substances in PPPs (such as imidacloprid and fipronil) is no longer approved in the EU, this is not the case in overseas countries that grow produce for export to and consumption in the EU. Food residue data collected by EFSA (2021[1]; 2022[2]) demonstrates that this input to WWTWs through human excreta may be important. Data for 2019 indicate that food residues may be 1.15 (middle bound) to 2.3% (adjusted upper bound) of the ADI, reported as 0.06 mg/kg bw per day. **Proposed change:** Proposed for additional consideration	Partly accepted. Thank you for highlighting the references. No changes to the table are deemed necessary, although the suggested references have been included in the discussion in section 6.1.1 of the RP.
391 and ff Table 4	10	**Comment:** Need a footnote noting that home and garden PPP uses may also have registered and while smaller than the agricultural uses may be significant (see below point related to section 6.2 and 6.3). **Proposed change:** Please add a footnote	Not accepted. Please note that the table only gives a general overview on the approval status of active substances and is not intended to give detailed information on registered products. No changes to the table are therefore deemed necessary.
424	10	**Comment:** Due to the risk that bees and other pollinators are exposed to outdoor plants treated with PPPs containing Fipronil and Imidacloprid corresponding PPPs (foliar applications, seed	Partly accepted. The CVMP acknowledges the comment. The last sentence has been amended to account for the continuing effectiveness.

[1] EFSA (European Food Safety Authority), Carrasco Cabrera, L and Medina Pastor, P, 2021. The 2019 European Union report on pesticide residues in food. EFSA Journal 2021;19(4):6491, 89 pp. https://doi.org/10.2903/j.efsa.2021.6491
[2] EFSA (European Food Safety Authority), Carrasco Cabrera, L and Medina Pastor, P, 2022. The 2020 European Union report on pesticide residues in food. EFSA Journal 2022; 20(3):7215, 57 pp. https://doi.org/10.2903/j.efsa.2022.7215

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		treatments) have been banned. Exposure of cats and dogs to pollinator can however be neglected as the fur of animals does obviously not serve bees as source for nectar or pollen. It is inappropriate to speculate that low cost is the main reason that these and other molecules are still used in VMPs. There are several other reasons such as high efficacy and/or easy application that play a role for customer preference. **Proposed change:** Please remove the last part of the sentence "possibly because of their low cost".	Please note that developments regarding ease-of-use of specific products is already addressed in the preceding chapter. Please also note that this line only explains why neonicotinoids are being phased out as PPP and does not address possible exposure scenarios from treated dogs or cats. Furthermore, it has not yet been studied whether direct or indirect exposure of pollinators to active substances e.g., from excreta of treated cats and dogs can be neglected or not. This topic is addressed later in the document under 'Environmental exposure scenarios'.
461–464	10	**Comment:** The conclusion that an individual animal treatment plan might require veterinary advice is not mentioned in the chapters before. In line 321-325 it is mentioned that publicly available information is laid down on in the SPC an PI (Package Insert), information brochures and treatment recommendations such as ESCAAP (2022). These are valid sources for animal owners. It seems to be assumed, that the extent of off-label use could be quantified, if prescriptions status and distribution channels were harmonised within the EU/EEA. **Proposed Change**: Please remove lines 461-464 or consider rewriting based on solid information.	Accepted. The wording in lines 326–327 and 461–464 has been revised accordingly.
470	10	**Comment:** Abbreviation MAH already introduced. **Proposed change:** Sales data of ectoparasiticidal VMPs are usually not published in the public domain	Accepted. The CVMP acknowledges the comments. The text has been revised accordingly.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		by ~~marketing authorisation holders~~ **MAHs** and consequently, no…	
483 and ff Table 5	10	**Comment:** Column header of kg/year is misleading. Numbers provided for Imidacloprid and Fipronil by Perkins *et al*. (2021)[3] are estimates on the accumulated use over more than 10 years from 1997 – 2019(?) and not kg/year. **Proposed change:** Please correct the header either change to kg or reporting period.	Accepted. The reporting period has been verified and the text has been changed accordingly.
510	10	**Comment:** A focus and comparison of the amount of active used is misleading (Stanneck et al., (2012) and does not allow for a 'general assessment of the situation' as indicated in line 495. The collar containing imidacloprid provides for example much longer protection than spot-ons and more than 60% of the active is not released from the collar to the dog but remains in the collar (Stanneck et al. (2012)). **Proposed change:** Please add after "used in collars" the sentence, "**which however release the actives slowly over a much longer period than spot-ons and more than half of the active amount will not be released from the collar by end of its use.**	Partly accepted. The second part of the proposed sentence has been included. However, the CVMP is of the opinion that the release patterns are not of relevance in this context.
518	10	**Comment:** The time period associated with the reported usage of imidacloprid and Fipronil needs to be clarified i.e., **1997 – 2019(?)**. It should also be	Accepted.

[3] Perkins, R., Whitehead, M., Civil, W., & Goulson, D. (2021). Potential role of veterinary flea products in widespread pesticide contamination of English rivers. Science of The Total Environment, 755, 143560.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		verified if uses for other "minor companion animal species" are included in given numbers. **Proposed change:** Please revise the reporting period to defined years and do not include periods which are under question mark as this cannot give realistic amount sold. Please verify the given numbers.	The reporting period has been verified and the text has been changed accordingly.
522	10	**Comment:** The wording is unclear as "spot on collars" makes no sense. **Proposed change:** Please amend to clarify	Accepted. The sentence has been corrected.
536	10	**Comment: "**The fraction that actually ends up in the environment is not known" This sums up the whole issue. Any assumptions made on this data basis are not scientifically sound. **Proposed change:** Please add after this sentence "**Before working on an update of the ERA, ensure sound data are available, in particular with a demonstrated link of the antiparasitic's role in the global issue.**"	Not accepted. The update of the ERA (guidelines) is not within the scope of the mentioned paragraph. Please note that the preceding and following paragraphs clearly state that these are to be seen as exemplary calculations. Please also note that the principle of introducing assumptions, the application of a total residue approach and the use of market penetration and population data are common scientific practice in the establishment of predicted environmental concentrations. Industry is welcome to disclose global sales data if available to ensure that sound data are available to demonstrate or refute the link of antiparasitics in the global issue.
542–558	10	**Comment:** The four bullet points may be misunderstood, please clarify in each case if the	Accepted.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		number of animals quoted is the EU population or 5% of the EU population.	The text has been amended accordingly.
542-549	10	**Comment:** The presented worst case assuming that the total amount of imidacloprid contains in a collar or a spot-on would be released in the environment is incorrect. Published data by Stanneck *et al.* (2012) showed that more than 60% of the total amount remain in the collar at the end of efficacy duration (e.g. imidacloprid collars). It should be considered that the main fraction of the active remains in the collar. This reduces the emission to the environment from 9.5 to 3.8 tons. **Proposed change:** Please correct 9.5 to 3.8 tons and add the Stanneck (2012) reference.	Accepted. The paragraph has been amended as proposed.
559–562	10	**Comment: "**Based on data available to CAs, the magnitude of possible total emissions to the environment obtained for the exemplary substances fipronil and imidacloprid using the above worst-case assumptions gives an indication for the overall EU/EEA situation. Such estimations for other commonly used active substances such as some pyrethroids, organophosphates or carbamates are expected to be similar." Surely, pyrethroids, organophosphates or carbamates would be used as an alternative to fipronil and imidacloprid?	Partly accepted. The wording has been revised for clarification.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change: Please revise the statement accordingly.	
566–572, Figure 2	5	**Comment:** Figure 2: It has to be emphasised that environmental exposures of topical applications via the given indoor and outdoor scenarios are considered as very low comparing to dog bathing (indoor/outdoor) and swimming in open waters and as such don't have to be considered as significant contributors to the environmental hazard or risk assessment. **Proposed change:** a comment/asterisk to the figure where the most important exposure scenarios are highlighted should be added: Bathing of dogs indoor or outdoor is considered as the major environmental exposure scenario.	Not accepted. Please note that specific pathways have intentionally not been highlighted or weighted in the illustration because they may differ considerably depending on the active substance, product type and/or route of application and also based on regional differences. Only limited data from bathing and swimming experiments are available for most active substances in the public domain, if at all. Data on concentration levels in faeces and urine are even more scarce.
582–584	10	**Comment:** Speculative wording with no evidence. **Proposed change:** Please remove the reference or add data to support the claim.	Not accepted. The potential exposure of birds to contaminated dog hair used for nesting is part of the current scientific discussion. Please note that it is the purpose of this RP (amongst others) to communicate the CVMP's view on the current state of the scientific discussion. The following sentence clearly states that neither the importance nor the impact that the residues of antiparasitics from pets (from this pathway) may have on wildlife are known.
587–589	10	**Comment:** Mahefarisoa et al. (2021) describe the exposure of bees and pollinators only in the context of the treatment of livestock. Referencing the dust/air	Partly accepted.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		pathway from excreta or sludge in the context of pet treatment is thus inappropriate. **Proposed change:** ~~Another pathway that has been reported in conjunction with parasiticidal VMPs, and which may have an impact on bees and pollinators, is via dust/air from excreta or sludge (Mahefarisoa et al., 2021).~~ For ~~both~~ **this** pathway, neither the importance nor the impact that the residues of antiparasitics from pets may have on wildlife are known.	Information that the excreta from livestock is referred to in the mentioned paper is added for clarification.
626–632	10	**Comment:** It is likely that a significant fraction of the pet hair and animal skin abrasions lost on the floor, carpets and animal bedding is vacuumed and subsequently disposed to household waste and therefore will not reach the wastewater. **Proposed change:** Please add this comment in line 631 after the sentence ending with "effluents."	Accepted. The text has been amended accordingly.
647–648	10	**Comment:** It is unclear what it meant by "free-roaming pets" in the exposure context. If this means feral animals, it is unlikely they would be regularly treated with an ecto-parasiticide, and thus, it is inappropriate to include them for exposure assessment. **Proposed change:** Please revise and clarify this statement.	Accepted. Please note, that the term 'free-roaming' does not state the status of ownership (abandoned, community or privately owned) or whether they are feral or stray animals, but refers to (pet) animals that freely roam (instead of being kept indoors only). Please also note that stray animals are often treated by community organisations, municipalities and non-

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
			governmental organisations for public health and animal welfare reasons, as outlined in section 3.1. The text has been revised as suggested for clarification.
654–659	3	**Comment**: The swimming trial in a small water pool (Diepens et al. 2023) shows in a single experiment with only one fluralaner-treated dog that fluralaner is transferred to water. However, a comprehensive risk assessment, which takes into account dilution, transfer to sediments, etc., would be needed to predict concentration in surface water. It is also not reported whether the dog was treated with a spot-on product or with a systemic-acting formulation and after what time period following treatment the dog was allowed to swim. **Proposed change**: Please tune down the statement that fluralaner release from the treated dogs may result in water concentrations above regulatory limits.	Accepted. Thank you for your comment. The statement regarding the exceedance of the surface water limit has been removed.
656–659	10	**Comment:** Diepens et al. (2023) refer to a surface water limit of 0.47 ng/L for fluralaner. As source for this value Lahr et al. (2019) is referenced. Lahr et al. (2019) in turn refers to the "dossier data" as source for the PNEC for surface water and provides a value of 0.00047 µg/L (0.47 ng/L). However, this value is incorrect. "Dossier data", i.e., the EMA CVMP "EPAR for Exzolt" also cited in the reflection paper (https://www.ema.europa.eu/en/documents/assessment-report/exzolt-epar-public-assessment-report_en.pdf) clearly indicate the surface water PNEC	Accepted. Thank you for your comment. The statement regarding the exceedance of the surface water limit has been removed.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		of fluralaner to be 0.0047 µg/L (4.7 ng/L). Accordingly, the statement in the publication of Diepens et al. (2023) is incorrect that water concentrations are above the surface water limit. This should be corrected. **Proposed change:** Data supporting these assumptions are scarce, although data from a very recent swimming experiment in an artificial pool showed that the transfer of fluralaner from dogs to the aquatic environment **may occur (Diepens et al., 2023), however** ~~lead to~~ water concentrations ~~above~~ **were below the PNEC for surface water of** ~~the surface water limit of 0.47 ng/L~~ 4.7 ng/L.	
661–688	3	**Comment**: Imidacloprid and fipronil are also approved in ferrets. **Proposed change**: Include ferrets as a target species and source of environmental contamination with imidacloprid and fipronil.	Accepted. The text has been amended to include further target species.
664	10	**Comment:** Imidacloprid was on the WFD WL between 2016-2019. **Proposed change:** Please replace 2020 with 2019	Accepted. The text has been amended as proposed.
672	10	**Comment**: Given the use of imidacloprid as an active substance in plant protection products and biocides (authorisation extended to 31 December 2025) the phasing out of this use strongly reduced the emissions. Although individual MS are still permitting exceptional uses, reasoning that no valid alternative is	Partly accepted. Thank you for your comments. The paragraph has been revised as proposed.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		available. As such, actual neonicotinoid use in agriculture is higher than assumed based on the (theoretical) ban. See https://www.pan-europe.info/resources/reports/2023/01/banned-pesticides-still-use-eu In addition, use in greenhouses also provides important contributions to water concentrations: Greenhouse production contributes to pesticide occurrences in Swedish streams - ScienceDirect An assessment performed using data referred to the period preceding the phase out would overestimate actual risk. **Proposed change:** Please add a sentence in line 672: **However, sampling periods of active substances in surface waters may cover periods where significant non-VMPs were permitted (such as the imidacloprid data collected before phasing out of plant protection products, but noting that it is still authorised as a biocide) and don't allow conclusion on the contribution from VMPs.**	
674	10	**Comment:** Does not include use of products as an agrochemical under emergency release as well as glasshouse usage. **Proposed change:** Please include this as a contributing factor.	Accepted. The text has been revised as proposed.
674–677	8	**Comment**: Relating to the use in biocidal products the active substance imidacloprid is approved for non-	Partly accepted.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		professional users and for outdoor use (around buildings) as well (at least in Germany). **Proposed change** (if any):	The term 'professional (use)' has been deleted. Please note that no reference to indoor or outdoor use is given.
679–680	10	**Comment**: Imidacloprid was on the Watchlist of the WFD from 2016-1019. Currently it is not on the Watchlist. When decisions were made, plant protection products containing imidacloprid were available. The current WL list does include Fipronil but not Imidacloprid. (Commission Implementing Decision (EU) 2022/1307 of 22 July 2022). **Proposed change:** Please change to Imidacloprid was on the surface water WL from 2016-2019.	Accepted. The text has been amended accordingly.
677; line 1138; line 1194 747 766	10	**Comment:** The text implies that biocides are not a realistic source contributing to residues in wastewater treatment plant effluent as they are used by professionals and as baits. This does not come across in the PARs of biocidal products[4], which indicate that this source may be an important contributor to monitored environmental residues. **Proposed change:** Please consider biocidal products as other contributing sources in the discussion and not just VMPs	Accepted. The text has been amended for clarification and the paragraphs related to the contribution of biocides later in the document have been revised.
682–685 + line 2097	8	**Comment:** Relating to the use in biocidal products the active substance fipronil is approved for non-	Partly accepted.

[4] https://echa.europa.eu/de/information-on-chemicals/biocidal-active-substances/-/disas/factsheet/37/PT18

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		professional users and for outdoor use (around buildings) as well (at least in Germany). **Proposed change** (if any):	The paragraph has been amended to account for regional differences.
695–906	5	**Comment:** In the 4JDS monitoring of the Danube river was performed between 2007-2019. At the time of performed monitoring, Imidacloprid was approved and used as PPP (approval expired on 1.12.2020) and biocide at much higher quantities compared to VMP use. The monitored concentrations therefore are due to PPP and biocide usage rather than the VMP usage. Based on the current monitoring data the environmental exposure of imidacloprid via VMP is overestimated. Due to the banned use in the PPP, monitoring of rivers in the next years may reflect a more realistic exposure via VMP – even though imidacloprid exposure and sales data via biocidal products have to be also considered. Fipronil was approved and used as PPP (approval expired on 3.09.2017) for a greater time period during performing of monitoring. Currently it is still used as biocide, therefore an environmental exposure solely on its VMP usage is currently not possible. The presented environmental risk of both compounds is clearly overestimated and cannot serve as basis for establishment of a risk evaluation proposal for both compounds as VMP. We may end up that for future MA, the MAHs will be required to present ERA phase II	Not accepted. The comment does not correctly reflect the content of the chapter. Please note that lines 695–859 address available monitoring data and relevant interpretations of the authors, where available. Please also note that in lines 860–906 conclusions on all available data (not only monitoring data) on *environmental fate and exposure data* are presented. However, no *environmental risk assessment* or an inflated environmental risk for such VMPs is presented. Uncertainties regarding monitoring data are acknowledged and are discussed in more depth in this chapter and throughout the RP. No estimation or overestimation on the contribution of VMPs for cats and dogs are given. Based on available data, the CVMP merely concluded that a contribution cannot be ruled out. Please also note that the available data on the market share and the pet population numbers are strong reasons to question the validity of the current assumption that the *environmental exposure* from the use of VMPs in cat and dogs can be considered as negligible, and not the available monitoring data.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		due to the inflated environmental risk that was presented for VMPs in the reflection paper. **Proposed change** (if any): Environmental exposure conclusions for VMP used imidacloprid and fipronil based on the current monitoring data is not appropriate. In the reflection paper it should be stated that appropriate risk evaluation for determing the environmental contribution of fipronil and imidacloprid used as VMP will be investigated and included in the guideline before finalisation.	
719–724	3	**Comment**: It is not clear why "other sources of supply should be considered as well" when ectoparastical collars are stated as the only legal source for diazinon in this region. **Proposed change**: Please include a justification for this conclusion. What other sources of diazinon must be considered and what is the evidence?	Accepted. In some Member States, diazinon is still in use in ectoparasiticidal VMPs for food-producing animals (mostly sheep dips) as addressed in the introduction of the mentioned chapter. Furthermore, the CVMP cannot verify all (legal) sources for diazinon in this region, as the Danube river basin is also subject to exposure by non-EU/EEA countries. The text has been revised as suggested for clarification.
787–793	10	**Comment:** The critique by Perkins *et al*. stipulating that the model by Anthe *et al*. implies imidacloprid is released from pets treated by spot-ons into the environment for 24 h only, is incorrect. In the model it is assumed that the applied amount of imidacloprid is available for 4 weeks, which is the registered period of protection for the spot-ons. The average amount of Imidacloprid available per day equals the total	Accepted. The reference and a note that this in an ongoing scientific debate has been added.

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		amount applied in the month divided by 30. The total amount applied per month is calculated from the month of highest frequency of use (based on survey data). Finally, the daily average calculated by the model are compared with the chronic PNECs. This was published in a commentary in the Journal Environmental Sciences Europe (Valles-Ebeling *et al.*, 2021, https://doi.org/10.1186/s12302-021-00580-1), but has not been taken into account in the RP. The conclusion "the authors find that the model appears consistent with the conclusion that emissions from VMPs may greatly exceed ecotoxicological thresholds and contribute substantially to imidacloprid waterway pollution in the UK" is therefore premature. Furthermore, in their response, Valles-Elbeling et al refer to new data being submitted for publication, hence this is an unfinished debate. **Proposed change:** Please correct the sentence and add the above reference referring to ongoing scientific debate.	
820	10	**Comment:** Decimal separators in Table 8 should be periods. **Proposed change:** Please change to 29**.**7 and 16**.**0	Accepted. Table 8 has been amended accordingly.
857	10	**Comment:** Period at the end of sentence is missing. **Proposed change:** …compounds**.**	Accepted. The text has been amended accordingly.
882	10	**Comment:** Please note that in the Guldemond study, a cocktail of chemicals was detected in each of the	Not accepted.

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		birds investigated. This complicates causality assignments and only provides a snapshot. Making reference to this single study suggests that there may be a risk from CA parasiticides to *e.g.,* chicks, but firstly, this is only a single study and secondly causality could not be identified (as noted by the authors). **Proposed change:** Please either the text is revised, making it clear that a cocktail of residues was detected (and causality could not be attributed) or delete the text.	The RP clearly states that a causality could not be identified. Therefore, a change to the text is not deemed necessary.
885–886	10	**Comment:** the likelihood of free-roaming animals being treated with a parasiticide is much lower, compared with pets kept within the household. Whilst we acknowledge that uncertainties are discussed in this section, weight seems to be given to unlikely scenarios. **Proposed change:** Please delete the statement, as free-roaming animal treatment considered sporadic at best.	Partly accepted. Please note, that the term 'free-roaming' does not state the status of ownership (abandoned, community or privately owned) or whether they are feral or stray animals, but refers to (pet) animals that freely roam (instead of being kept indoors only). Please also note that stray animals are often treated by community organisations, municipalities and non-governmental organisations for public health and animal welfare reasons, as outlined in section 3.1. The text has been slightly revised for clarity.
940–1045	5	**Comment**: Environmental hazard information for imidacloprid and fipronil are given as EQS. According to Directive 2001/82/EC, Regulation (EU) 2019/6 and corresponding ERA guidelines, the calculation of risk	Partly accepted. Thank you for your comment. The CVMP agrees that a re-evaluation of risks for the use as pet VMP would be preferable instead of referring to EQS, NOECs, PNECs and

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		quotient RQ = PEC/PNEC represents the relevant characterisation or calculation of environmental risk for VMPs. Environmental quality standard (EQS) is a risk characterisation performed within Directive 2000/60/EC and should not be misused for ERA of VMPs. **Proposed change** (if any): Revaluation of risk for fipronil and imidacloprid used as VMP should be performed. Instead of EQS, NOECs, PNECs and RQs in line with the EMA/CVMP/ERA/418282/2005-Rev.1-Corr.1 should be used when referring to the ecotoxicological studies and risk characterisation.	RQs of other frameworks when discussing ecotoxicological studies and risk characterisation for the use as VMP. However, please note that the VICH and EMA guidelines do not provide guidance for an environmental risk assessment of products used for pets. Furthermore, the development of such a guidance is not within the scope of the present RP. To avoid any misunderstandings the paragraph has been revised introducing the term *Environmental Threshold Concentrations* (ETCs).
948	10	**Comment:** A reference to the WFD TGD 27[5] (section 2.8 pg 26 and 27) where the difference between EQSs and RACs are discussed should be made. Many "experts" do not seem to be familiar with the difference between these endpoints (RAC/PNEC/EQS) and that they can't necessarily be used interchangeably. Specifically, that their use is in relation to a specific Directive and this Directive along with its associated technical guidance typically mandates how they are derived, used and interpreted specific to the protection goals under that Directive. **Proposed change:** Please add the above-mentioned reference	Partly accepted. Thank you for your comment. Reference to WFD is not deemed necessary, however, the paragraph has been revised introducing the term *Environmental Threshold Concentrations* (ETCs) to avoid any misunderstandings.

[5] https://circabc.europa.eu/sd/a/0cc3581b-5f65-4b6f-91c6-433a1e947838/TGD-EQS%20CIS-WFD%2027%20EC%202011.pdf

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952	10	**Comment:** Table 7 contains an error. The PNEC surface waters for fluralaner is incorrectly presented with 0.00047 µg/L (0.47 ng/L), the correct value is 0.0047 µg/L (4.7 ng/L). The correct value is provided in the EMA CVMP "EPAR for Exzolt" cited in the reflection paper as EMA/CVMP (2022) (https://www.ema.europa.eu/en/documents/assessment-report/exzolt-epar-public-assessment-report_en.pdf). In contrast, the second reference cited as source for the PNEC surface waters for fluralaner, Lahr et al. (2019), provides the incorrect value of 0.00047 µg/L (0.47 ng/L). Lahr et al. (2019) thereby is a secondary reference only as it refers to the "dossier data" as source for the PNEC for surface waters. Obviously, Lahr et al. (2019) made a typing error when transcribing the PNEC from the "dossier data", i.e., the EMA CVMP "EPAR for Exzolt", into their report (in contrast to the PNECs for soil and sediment which were transcribed correctly). It would be preferable for the reflection paper to refer to primary data sources only (in this case the EMA CVMP "EPAR for Exzolt") and to avoid the inclusion of secondary data sources to prevent potential presentation of incorrect values. Accordingly, in Table 7 the PNEC surface waters for fluralaner has to be corrected to 0.0047 µg/L and the reference of Lahr et al. (2019) has to be deleted. **Proposed change:**	Accepted. Thank you for your comment. The text has been amended as proposed.

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		PNEC[7] (surface waters) | | | **0.0047** µg/L | (~~Lahr *et al.*, 2019;~~ EMA/CVMP, 2022)	
972–975	10	**Comment:** The sentence is somewhat unclear. **Proposed change:** Examples for the "most commonly used test species for aquatic toxicity to invertebrates" shall be provided (*Daphnia*?) as well as for the "species commonly found in many freshwater systems".	Not accepted. Details on the test species concerned can be found in the reference cited. Therefore, no amendments to the text are deemed necessary.
989	10	**Comment:** The text on the fate of Imidacloprid is incomplete. Imidacloprid has the potential to be persistent in soil and sediment. This is significant as residues from agricultural usage may slowly contribute to environmental concentrations measured in SW for a number of years after the last use of Imidacloprid containing PPPs. This principle has been demonstrated by Boye *et al.* (2022)[6] in Sweden for uses of Imidacloprid in greenhouses, concluding that "One possible explanation for the high detection frequency of imidacloprid is that this substance is quite persistent in both water and soil (DT50=90 days and 77–82 days, respectively (EFSA, 2014b)), meaning that previous use in greenhouses (prior to the study period) could have contributed although not [been] included in the pesticide application journals."	Partly accepted. Thank you for your comments. Additions have been made with regard to the moderate to very high persistence of imidacloprid in soil and dark natural water sediment. Please note that the paragraph on environmental behaviour is not intended to be exhaustive. As indicated in the introductory paragraphs in chapter 5, the brief outlines given are intended to bring the measured environmental concentrations of the case studies into context and to facilitate the discussion in section 6. Please also note that it is outside the remit of the CVMP to confirm or refute the contribution of PPPs, biocides or other products to environmental concentrations of active substances. As highlighted in the discussion, the CVMP is aware that the contribution of (ectoparasiticidal) VMPs to

[6] Boye, K., Boström, G., Jonsson, O., Gönczi, M., Löfkvist, K., Kreuger, J., 'Greenhouse production contributes to pesticide occurrences in Swedish streams', Sci Total Environ, Vol. 809, 2022, 152215. DOI: https://doi.org/10.1016/j.scitotenv.2021.152215.

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		The fate of Imidacloprid in soil and water systems is reported by EFSA (2008)[7], following use of Imidacloprid as an insecticide in agricultural settings. It is clear that Imidacloprid is persistent in soil. In laboratory aerobic soil studies (four soils), Imidacloprid degradation was slow (DT50 99 – 129 days; geometric mean 118 days, normalised to pF2 and 20°C). Degradation under field conditions (nine sites) was also slow (DT50 27 – 180 days; median 78 days, normalised to pF2 and 20°C); such that accumulation studies were also conducted. Accumulation at three sites were investigated in Germany following six annual applications to grass under trees in orchards (plateau reached after three years, with a non-normalised Imidacloprid DT50 of 182 days); at two sites in UK, following six Imidacloprid annual applications of barley seed treatment (where plant residues were ploughed in every year), no plateau was reached in the six years, and the non-normalised DT50 was 1333 and 1268 days. Consequently, it is clear that significant declining soil residues of Imidacloprid could still be present in soil many years after the last agricultural application is made, and hence available to move to surface water. In addition, Imidacloprid degradation in soil does not mineralise completely (only 3.3 – 16.6% of applied	environmental concentrations of imidacloprid in surface waters or wastewater effluents cannot be quantified, albeit a relevant contribution cannot be ruled out.

[7] EFSA, 'Conclusion regarding the peer review of the pesticide risk assessment of the active substance imidacloprid', EFSA J, Vol. 6, No. 7, 2008, pp. 1–120. DOI: https://doi.org/10.2903/j.efsa.2008.148r.

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		Imidacloprid converted to carbon dioxide after 100 days at 20°C), and non-extractable residues are moderately large (17 – 27% of applied Imidacloprid after 100 days). It is reasonable to assume that non-extractable residues could slowly release further Imidacloprid over time. In water/sediment systems, Imidacloprid can also generate large non-extractable residues (up to 66% of applied Imidacloprid); however, although photolysis of Imidacloprid in soil was not found to be a significant degradation pathway, photolysis in aqueous systems could potentially be significant, and there is therefore uncertainty as to how significant the Imidacloprid - releasable component of sediment non-extractables would be. However, long-lived cryptic declining residues in sediment could be a low-level source of Imidacloprid for several years after the last agricultural application.	
1037–1039	10	**Comment:** Information on sarolaner metabolism is available in the dossier; the statement here is incorrect. **Proposed change:** Please correct after review of the relevant studies in the dossier.	Not accepted. Please note that data available in the EPAR for Simparica (EMA/CVMP, 2020c) state that the primary route of elimination is biliary excretion of the parent molecule, with minor contributions from metabolic clearance, which is also reflected in the annex. Therefore, no amendments to the text are deemed necessary.

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1042–1045	3	**Comment:** The use of fluralaner in poultry might have a greater environmental impact than the use of this same drug in cats and dogs. **Proposed change**: The reflection paper should include a rough assessment of how the use of fluralaner in poultry compares to the use of this drug in cats and dogs in terms of environmental contamination. This assessment should not only include the current but also predict the future use of fluralaner against the red mite in poultry.	Not accepted. Please note that only the environmental risk assessment of ectoparasiticidal substances used in VMPs for cats and dogs are within the scope of the present RP which is not intended to refute or confirm whether the contribution from other products to environmental concentrations are more or less significant. Therefore, no amendments to the text are deemed necessary.
1042–1045	10	**Comment:** The PNEC surface waters (or hazard limit) for fluralaner is incorrectly presented with 0.00047 µg/L (0.47 ng/L) by Lahr et al. (2019). Lahr et al. (2019) is a secondary reference only as it refers to the "dossier data" as source for the PNEC for surface waters. Obviously, Lahr et al. (2019) made a typing error when transcribing the PNEC from the "dossier data", i.e., the EMA CVMP "EPAR for Exzolt", cited in the reflection paper as EMA/CVMP (2022) (https://www.ema.europa.eu/en/documents/assessment-report/exzolt-epar-public-assessment-report_en.pdf) into their report (in contrast to the PNECs for soil and sediment which were transcribed correctly). It would be preferable for the reflection paper to refer to primary data sources only (in this case the EMA CVMP "EPAR for Exzolt") and to avoid the inclusion of secondary data sources to prevent presentation of incorrect values. The correct value for the PNEC (or hazard limit) is provided in the EMA	Accepted. The PNEC value has been corrected accordingly.

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		CVMP "EPAR for Exzolt" with 4.7 ng/L (0.0047 µg/L). The conclusion presented in lines 1042-1045 therefore needs to be corrected. Moreover, it is astonishingly in general that the reflection paper lists a hazard limit provided in a research report (Lahr et al., 2019) that is 10-fold lower than the PNEC defined in the EMA CVMP "EPAR for Exzolt". It would be preferable for the reflection paper in general to refer to EMA CVMP documents (if available) rather than to other sources, especially in case of conflicting data. **Proposed change:** For fluralaner, ~~Lahr et al. (2019)~~ **EMA/CVMP (2022)** defined a hazard limit of **4.7** ng/L for surface waters based on a chronic NOEC of 47 ng/L in *Daphnia magna*, which was determined in the frame of the authorisation of a VMP indicated for the treatment of the red mite (*Dermanyssus gallinae*) in poultry, to date the only use of an isoxazoline in food-producing animals in the EU/EEA (EMA/CVMP, 2022).	
1052–1054	10	**Comment:** While stating that afoxolaner is the only isoxazoline to undergo metabolism, into water soluble metabolites, it then goes on to say, "it is reasonable to presume that they (isoxazolines) would all show a similar environmental behaviour to fluralaner". We don't think this is necessarily reasonable to assume, particularly if it comes to concerns around bioaccumulation (with fluralaner being shown to be non-bioaccumulative, non-B).	Partially accepted. The paragraph has been partly reworded. Having said this, please note the environmental behaviour of afoxolaner has not been studied. According to information in the EPAR for NexGard (EMA/CVMP, 2020b), it is true that afoxolaner is metabolised into various metabolites. However, the major elimination pathway is still biliary excretion (about 30%) and only to a lesser extent via urine (renal clearance less than 0.01% of the total clearance). Therefore, the

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change: Data on the environmental behaviour of other isoxazolines could not be found, ~~although it is reasonable to assume that they would~~ therefore it remains unclear if they show a similar environmental behaviour to fluralaner.	assumption that afoxolaner is relevantly metabolised into water soluble metabolites does not hold true.
1101–1102	10	**Comment:** This paragraph might be improved by differentiating isoxazolines and the variance in principal routes of excretion (i.e., faeces vs urine). **Proposed change:** Please revise that statement taking the above in consideration	Partially accepted. The principal routes of excretion (faeces and urine) are addressed in the lines thereafter and the CVMP feels that further details on the variance in principal routes of excretion would not provide an added value to this chapter. However, the paragraph has been amended to account for other routes of application of products containing systemically-acting substances. Please note that isoxazolines are not the only systemically acting active substances to be considered.
1140–1145	10	**Comment:** *"The use of these active substances in VMPs for cats and dogs can be an additional source of environmental exposure in urban areas. In measurements where imidacloprid or fipronil were detected in WWTPs, the source of the active substances (VMP, PPP or biocide) cannot be differentiated, but the intricate route of the use in PPPs and the limited emissions from biocides indicate that the use as in VMPs for companion animals contribute to the presence in urban wastewater. Modelled data available in public literature aimed to prove the contrary, but these results were challenged*	Accepted. The additional reference and the ongoing scientific debate have been taken into account.

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		by other authors highlighting shortcomings in the methodology used.” **Proposed change:** Please refer to comment re Lines 787-793. Consider that shortcomings of the model were re-evaluated concluding that there were no shortcomings, and further data were to be offered for publication.	
1167–1168	10	**Comment**: It is stated that no information is available about the presence of substances like imidacloprid in sewage sludge. However, this is not correct. Information about the concentration of imidacloprid in sewage sludge is available in report 169/2020 of the German UBA about the release of biocidal products into the environment by means of the STP (UBA Texte “Belastung der Umwelt mit Bioziden realistischer erfassen - Schwerpunkt Einträge über Kläranlagen | Umweltbundesamt)”). **Proposed change:** Please correct the statement	Accepted. The sentence has been corrected as suggested. Furthermore, the research article has now been included in section 4.3. and is referred to in section 6.1.1.
1180–1182	10	**Comment:** The sentence is incorrect as it based on the incorrect PNEC surface waters for fluralaner presented in Table 7. Considering the correct PNEC of 0.0047 µg/L as provided in the EMA CVMP “EPAR for Exzolt”, cited in the reflection paper as EMA/CVMP (2022), the toxicity of isoxazolines is in the same range as for imidacloprid and fipronil. **Proposed change:** Ecotoxicological data for isoxazolines is scarce, but the information available	Accepted. The text has been amended as proposed.

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		points to a ~~higher~~ **similar** toxicity to aquatic invertebrates ~~with NOECs in the order of 1181 centesimal µg/L~~.	
1194	10	**Comment:** The statement that PPP contributions to WWTWs is low does not appear to consider home and garden usage of biocides. While the text below relates to the UK where such usage data is available, this is likely to be broadly applicable to many parts of the EU, where the authorisation of imidacloprid as a biocide has been further extended until 31 December 2025. • There are no readily available sales or usage data for the use of IMI containing products by amateurs around their homes and gardens, however, the potential risk that this source presents to surface waters may be characterised by other datasets that are available. • The UK Pesticides Strategy (Defra, 2006) estimated that 6-7 million people (~10% of the population; ~28% of households) used pesticides around their homes and gardens concluding "that the total quantity of pesticide used by amateurs, while still small in relation to farm use, is significant".	Partially accepted. Some clarifications have been added to the document as suggested.

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		• The UK Pesticide User Habits Survey (2016)8 indicates the following: ○ 53% of respondents use insecticides with around a third (38%) using ready-to-use products only, compared to 18% using concentrate products only, while 40% stated they used both ready-to-use and concentrate products. ○ 2% would dispose of leftover pesticides (both ready to use and concentrate products) down the drain/sink on disposal; ○ 37% of ready-to-use product users rinse the containers before recycling the bottle; ○ 60% of concentrate product users rinse the containers before recycling the bottle; ○ 22% store products for > 3 years; This demonstrates that up until 2015, and possibly well beyond as amateur users are less likely to know that a product registration has been withdrawn, this source may have been important as it constitutes direct disposal, in some cases of concentrated product or the container washings of concentrated products, down the drain to surface water via wastewater treatment works.	

[8] https://www.hse.gov.uk/pesticides/resources/G/Garden_User_Habits_Survey_Report_2016.pdf

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		Proposed change: Please revise that statement taking the above in consideration	
1213 and ff Section 6.2 and 6.3	10	**Comment**: There needs to be some acknowledgement of the potential use of mixing zones in interpretation of monitoring data associated with point sources, especially within the context of the WFD. Under the EQS Directive (2008/105/EC) Part B Article 19 mixing zones can be considered as part of the data interpretation (see below): "*In the vicinity of discharges from point sources, concentrations of pollutants are usually higher than the ambient concentrations in water. Therefore, Member States should be able to make use of mixing zones, so long as they do not affect the compliance of the rest of the body of surface water with the relevant EQS. The extent of mixing zones should be restricted to the proximity of the point of discharge and should be proportionate. In accordance with Article 3(4) of Directive 2000/60/EC, Member States should ensure, as appropriate, that the requirements for the achievement of the environmental objectives set out in Article 4 of that Directive are coordinated for the whole of the river basin district, including the designation of mixing zones in trans boundary water bodies.*" **Proposed change:** Please revise that statement taking the above in consideration	Not accepted. As explained in chapter 6.1., the limited data available do not allow for a quantitative environmental risk assessment. Therefore, the CVMP opted for a qualitative discussion of the environmental risks of VMPs containing (ecto-)parasiticidal substances. A consideration of mixing zones in such a qualitative assessment and a revision of the statement are thus not deemed necessary.

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1218–1226	10	**Comment:** *"For collars the following (template) wording should appear: " is toxic for aquatic organisms. Remove the collar before allowing the dog to swim and before bathing the dog to avoid adverse effects on aquatic organisms". The CVMP "Reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products" (EMA/CVMP/ERAWP/409328/2010; (EMA, 2012), which is currently under revision, recommends the above wording and considers the measure in line with the current ERA guidance, i.e. the RMM is able to mitigate the exposure of the VMP to the environment and it is possible to demonstrate the effect of the proposed RMM by re-evaluating the exposure assessment with the proposed risk mitigation measures included."* Immersion / bathing studies conducted for some collars allowed to determine the amount of active substances released from the collars into water when dogs swim / bath (https://enveurope.springeropen.com/articles/10.1186/s12302-021-00580-1/tables/2). **Proposed change:** Due to the nature of the product and the slow release from the collar matrix, limited release can be expected. Where available, these types of studies should be considered in the risk assessment before decision on RMM.	Not accepted. Please note that this is a general product-class-based RMM applicable to collars. Specific deviations for individual products are always possible on a case-by-case basis if sufficiently justified with data. However, such product-related discussions are not within the scope of the present RP and should be conducted in the frame of marketing authorisation or variation procedures. Therefore, no changes to this paragraph are deemed necessary. Please note that the reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products (EMA/CVMP/ERAWP/409328/2010) is currently under revision and will address some of these points. Therefore, no amendments to the text are deemed necessary.

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1280–1283	5	**Comment:** As outlined in Section 4.4., the conclusions that pet VMPs contribute to surface water concentrations of these active substances are equivocal. While this is not clear, it is not advisable to raise awareness of the environmental hazards of these VMPs to the public such as pet owners and pet associations. This measure could lead the discussion outside the scientific terms. **Proposed change**: Deleting these lines.	Not accepted. While the CVMP acknowledges that the actual contribution of these VMPs to surface water concentrations or to the terrestrial compartment cannot be quantified or are unknown (as concluded in multiple occasions within the RP), the insecticidal and acaricidal properties, however, are very clear. Therefore, no changes to this paragraph are deemed necessary. Please note that the sustainable and prudent use of pharmaceuticals should always be encouraged considering a 'One Health' approach. Public awareness and public education are key elements in such efforts, which includes being transparent to pet owners (and veterinarians) on known environmental properties/hazards of active substances used in pet VMPs. This is considered beneficial for the promotion of a responsible use. Therefore, no amendments to the text are deemed necessary. However, to improve the structure and clarity of the document, the suggestions have been moved to chapter 6.4.
1283	10	**Comment**: The EU Strategic Approach to Pharmaceuticals in the Environment not only seeks to reduce emissions to WWTWs and promote the development of medicines that are more easily removed during treatment but also plans to better understand removal of substances during treatment as	Not accepted. Please note that wastewater treatment plants and their treatment technologies are outside of the remit of the CVMP. The reference to the revision of the Urban Waste Water Treatment Directive (UWWTD, Council Directive 91/271/EEC) is appreciated, but it has no impact on the need to further

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		well as upgrading WWTWs where necessary (see page 10) e.g. *"In relation to urban wastewater treatment:* *- Use Union programmes to invest in technologies to improve the efficiency of removal of pharmaceuticals (and antimicrobial resistance genes);* *- As part of the study supporting the evaluation of the existing urban waste water treatment legislation, assess whether it sufficiently controls pharmaceutical emissions and investigate the feasibility of upgrading selected urban waste water treatment plants to more advanced treatment technologies;* **Proposed change:** Please revise taking the above in consideration	investigate the potential environmental risk of pet parasiticides. No changes to this paragraph are deemed necessary. However, to improve the structure and clarity of the document, the suggestions have been moved to chapter 6.4.
1292–1295	5	**Comment**: Which "non-medical preventive measures" could be implemented? Examples will be appreciated. In some cases, these measures could lead to reduction in the use of VMPs, while in other cases it might not lead to reduction if the VMP shall still be used. **Proposed change**: Using the word "rationalised" instead of "reduced". Adding examples of non-medical preventive measures.	Partly accepted. The sentence already reads 'may be reduced', which accounts for situations where this might not apply. Examples for non-medical measures are given in chapter 3.2 under the heading of 'Prudent use, treatment plans and owner compliance'. That being said, examples of non-medical preventive measures are now also included here. To improve the structure and clarity of the document, the suggestions have been moved to chapter 6.4.

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1296–1297	10	**Comment:** The CP does not clearly explain what is meant by the holistic treatment concept of stray and feral animals. The reflection paper highlights the significant role rescue and stray animals may play in transmitting human and animal disease, particularly when translocated between countries. But is the paragraph, for example, suggesting better guidance or non-therapeutic interventions such as better control of movement as an alternative or additional approach. **Proposed change:** more clarity would be helpful	Accepted. The paragraph has been revised to give more clarity. To improve the structure and clarity of the document, the suggestions have been moved to chapter 6.4.
1314 & 1317; Line 1456 & 1459	10	**Comment:** There is a need for the development of clear guidelines for the analysis of public monitoring data as part of any pharmacovigilance or state of the environment assessment. While some Directives and their associate technical guidance mandate specific approaches, these may not always be appropriate e.g. the QA/QC Directive (2009/90/EC) outlines the use of the substitution approach when dealing with left-censored data (data <LOQ/LOD). However, this approach has been shown to lead to significant bias in results under certain conditions. The JRC acknowledged this issue in the recent round of Draft PS dossiers (e.g., see Imidacloprid draft dossier) and used an alternate non-parametric approach. Analyses in reports and published literature capture a range of data analysis and risk assessment inconsistencies, for example comparing an EQS-AA with individual measurements rather than an annual average or	Not accepted. The comment is acknowledged. The development of guidelines for the analysis of monitoring data is not within the scope for this RP. These paragraphs just state that pet VMPs should be considered. No changes to these paragraphs are deemed necessary.

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		calculating an annual average from 2 or 3 values rather than, for example, 12 samples required for a robust assessment as required by the WFD for priority substances. **Proposed change:** Please revise that statement taking the above in consideration	
1327–1328	10	**Comment:** "Some data gaps" may be a significant understatement - currently there remains a significant absence of evidence supporting specific environmental risks from current use of specific companion animal ectoparasiticides. **Proposed change:** please replace "some" with "significant"	Not accepted. Please note that the conclusions on environmental risks are based on effects and exposure data. The data on environmental effects (insecticidal and acaricidal activity) and on properties of substances of concern (many can be classified as persistent and/or as PFAS) are available for most 'major use' substances. Please also note that environmental exposure data for risk assessments are typically are not determined with evidence from monitoring data, but on the basis of exposure calculations. Models for such exposure calculations are currently being developed, as stated above. Therefore, the current wording is considered appropriate.
1330–1334	10	**Comment:** A call for better education of pet owners using these products is needed in this section too. **Proposed change:** Please revise that statement taking the above in consideration	Accepted. A statement on educational measures to improve owner compliance with the correct handling instructions has been included. To improve the clarity of the document, chapter 6.4. has been restructured.

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1330–1335	10	**Comment***:* The industry recommends pet owners to regularly visit a veterinarian. A discussion on a tailored treatment plan is common practice. However, proper treatment does not depend on prescription only. With regards to the environment, veterinarians, retailers and industry should provide appropriate information to reduce potential risk to the environment. **Proposed change:** Please change sentence to: A better regulation of the sale of these products (e.g. advertisement control) and information campaigns ~~or the consideration of environmental safety when assigning the prescription status~~ may be beneficial, as this would motivate pet owners and caretakers to have ~~veterinarians prescribe~~ tailored treatment plans suited to the specific needs of the individual companion animal or the stray animal populations in a specific region.”	Partly accepted. It is acknowledged that veterinarians, retailers and industry could and should provide appropriate information to reduce potential risks to the environment, that proper treatment does not solely depend on prescription status and that industry recommends pet owners to regularly visit a veterinarian. Nevertheless, the assignment of a prescription-only status should not be disregarded as an option to increase prudent use and to ensure environmental safety, since this is certainly a more effective measure to motivate pet owners and caretakers to seek veterinary advice than a mere recommendation. Chapters 3.2 and 6.4 have been revised to clarify the relevance of the environmental safety profile of a VMP on the prescription status and the benefits of a prescription-only status from an environmental safety point of view. To improve the clarity of the document, the chapter 6.4. has been restructured.
1346–1352	10	**Comment:** “The RMM specified for spot-on VMPs usually recommends that animals should not enter surface waters 48 hours following the treatment. There is no temporal restriction for washing treated animals for environmental safety reasons, during which the release could be higher. The assumption of the environmental safety of the 48-hour period as a general precaution does not appear to be based on a product-specific scientific assessment and it is	Partly accepted. Please note that this is, as indicated in the RP, a product-class-based precautionary RMM applicable to spot-on products in general. Specific deviations for individual products are and have always been possible on a case-by-case basis if sufficiently justified with data. The default value of 48 h has been introduced by the reflection paper on risk mitigation measures to avoid the need for bathing studies to

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		doubtful if it applies to all active substances and all formulations, especially considering that, for some VMPs, a longer period is recommended to maintain efficacy.″ **Proposed change:** There are examples with a longer or shorter period than only 48 h based on product specific assessment. EMA (European Medicines Agency) (2020) Summary of product characteristics Advocate. https://www.ema.europa.eu/en/documents/product-information/advocate-epar-product-information_en.pdf https://www.ema.europa.eu/en/medicines/veterinary/EPAR/stronghold#product-information-section	determine the number of days. However, such product-related discussions are not within the scope of the present RP. Please note that the reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products (EMA/CVMP/ERAWP/409328/2010) is currently under revision and will address some of these points. Some slight changes have been made to account for the comment made. Chapter 6.4. has been restructured to improve the clarity of the document.
1372–1375	10	**Comment:** The economic value statement … "showing that the number of available ectoparasiticidal VMPs for companion animals has significantly increased in recent years which in turn confirms their economic value for the pharmaceutical animal health sector" has no bearing on the potential risk which such products may present. Increased economic value results from enhanced efficacy (price-point considerations) and not on higher sales volumes; a better product replaces one which is less efficacious and can therefore achieve higher financial returns. **Proposed change:** Please delete the statement	Not accepted. Please note that this paragraph describes the current situation in Europe regarding the cat and dog population as well as different aspects regarding authorised ectoparasiticidal VMPs. The economic value of these products for the animal health sector is just one of many aspects highlighted. No conclusions on actual sales volumes and even less on the environmental risks are drawn in this paragraph and later in the document (7. 'Conclusions on current ERA approach'). However, please note that the market share and the pet population numbers are a strong reason to question the validity of the assumption that the environmental exposure from the use of VMPs in cats and

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			dogs can be considered to be negligible. Therefore, a deletion of the statement is not deemed necessary. CVMP appreciates to receive sales data per volume. Industry is welcome to disclose sales data to prove the contrary.
1396	10	**Comment:** "for example monitoring for active substances solely used in pet VMPs". The nature of the "monitoring" is not specified e.g., sales volumes, prescriptions issued, environmental monitoring etc. **Proposed change:** Please clarify what is meant by "monitoring"	Accepted. Thank you for your comment. A clarification has been added.
1400–1401	5	**Comment**: As outlined in General Comments, further monitoring would be necessary before establishing conclusions concerning the environmental risks of ectoparasiticidal VMPs for cats and dogs. While this is not clear, it would be advisable deleting these lines. **Proposed change**: Deleting these lines.	Not accepted. The mentioned lines refer to the validity of the assumption that the environmental exposure from the use of VMPs in cat and dogs can be considered as negligible. Please note that the conclusions on environmental risks are based on effects and exposure data. Please also note that environmental exposure data for risk assessments are typically not determined using evidence from monitoring data, but on the basis of exposure calculations. Models for such exposure calculations are currently being developed, as stated above. Therefore, the current wording is considered appropriate.
1400–1401	10	**Comment:** CVMP concludes that certain CA VMPs should not stop in Phase I. However, there is no further information presented on how a Phase II risk assessment should be performed.	Partly accepted.

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		Proposed change: Additional wording needs to be added to explain that suitable exposure scenarios will be developed in order to perform a Phase II ERA.	The CVMP concludes that the current approach should be revisited. It is not within the remit of the CVMP to unilaterally change internationally harmonised guidance. Please note that key considerations as to which data gaps would need to be filled to achieve a better understanding of the exposure pathways and to allow for a specific product-based risk assessment as well as further regulatory options are highlighted in the following paragraphs. An additional paragraph on the next steps has been added at the end of chapter 7 to give clarity on the anticipated way forward.
1410	10	**Comment:** Protection goals are not actually defined within this reflection paper. Has a risk to the environment actually been identified? **Proposed change:** The desired outcome of introducing further risk assessment beyond Phase I needs to be clearly stated.	Not accepted. Please note that chapter 7 refers to protection goals, stating that surface waters (including sediments) are possibly the most important receiving compartment, since most exposure pathways end up there. However, future evaluations of protection goals might go beyond the impact on aquatic arthropods. Please also note that, as detailed in chapter 6.1, the CVMP opted for a qualitative discussion of risks, to achieve the objectives defined in the aims of the RP, concluding that, on the basis of the available information, it cannot be ruled out that some ectoparasiticidal VMPs used in cats and dogs (at least at higher consumption levels) contribute to the concentrations of ectoparasiticidal substances that pose a risk to the aquatic environment in the vicinity of WWTP discharges.

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			Please also note that specific product-based risk assessments are part of marketing authorisation dossiers and that specific requirements are not within the scope of this RP. The latter would thus need to be discussed on a case-by-case basis in the frame of a relevant regulatory procedure. An additional paragraph on the next steps has been added at the end of chapter 7 to give clarity on the anticipated way forward.
1411–1414	10	**Comment:** *"Although spot-on products and tablets are the most commonly used formulations, the amount of active substances used are largely influenced by the sale of collars, which contain greater amounts of active substance than cutaneous and oral formulations, although the amounts actually released from the collars to the animal and subsequently to the environment before disposal are unknown."* Although the amounts of active substance in a collar may be greater than in spot-on formulations, published data (Stanneck et al. 2012) showed that a large amount of the active substance is not released from the collar matrix during the registered period of efficacy. **Proposed change:** Please refer to the publication.	Partly accepted. The wording has been revised in line with the conclusions drawn in chapter 4.4.
1424–1425	10	**Comment:** The sentence is incorrect as fluralaner is authorised in a VMP for a food-producing animal. Accordingly, environmental safety data exist, which were evaluated by the EMA CVMP (EMA CVMP "EPAR	Partly accepted. The text has been amended accordingly.

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		for Exzolt", cited in the reflection paper as EMA/CVMP (2022)). **Proposed change:** Knowledge gaps exist predominantly for those substances, which are only authorised in VMPs for companion animals, i.e. **most** isoxazolines **except fluralaner**.	
1436–1450	3	**Comment**: A substantial number of people are not able to understand a simple text such as the owner information that accompanies veterinary medicinal products. **Proposed change**: Please consider recommending a leaflet summarizing the most important risk management measures (for example removing the ectoparasiticidal collar before swimming) in self-explanatory visual displays.	Not accepted. Your comment is acknowledged and information campaigns by stakeholders are appreciated. Product-specific requirements, however, will need to be discussed on a case-by-case basis and general changes to the requirements for product literature are outside the scope of this RP. Therefore, no changes to this paragraph are deemed necessary.
1444	5	**Comment:** Same as lines 1292-1295 **Proposed change**: Using the word "rationalised" instead of "reduced".	Not accepted. The sentence already reads 'may be reduced', which accounts for situations where this might not apply. An amendment of the text is therefore not deemed necessary.
1452–1465	10	**Comment:** *"Considering that (i) the bans restricting the use of active substances such as imidacloprid and fipronil in PPPs and biocides have not yet been fully implemented;"* There is no decision to ban the biocidal uses of imidacloprid (authorisation extended until 31 December 2025) and fipronil. Please refer to the	Partly accepted. The wording has been adapted accordingly.

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		previous comments with regards to the emission based on biocidal use.	
1455–1465	10	**Comment:** "CVMP supports the continuation of monitoring environmental concentrations of parasiticides used in cats and dogs. The design of future monitoring programs for multiple-use substances and the interpretation of data should consider the use of such VMPs and that general knowledge gaps exist regarding the bioavailability of such substances in water. In addition, specific ad-hoc monitoring studies carried out at potential hotspots in urban catchment for specific (ecto-)parasiticidal active substances used in VMPs for cats and dogs are needed. Such targeted measurement programs should include sediments and sewage sludge. To support monitoring by environmental managers and the research community, marketing authorisation holders are encouraged to share details on analytical methods (and standards). The impact of excreta from treated animals on the terrestrial compartment, for example in urban and peri-urban ecosystems, should also be part of reflections on future measurement programs and scientific studies." It is essential that any new monitoring studies are well-designed, if their results are to be used as a basis for determining whether further regulation of companion animal parasiticides is warranted. Many	Not accepted. The comment is acknowledged. However, please note that the design of specific monitoring programmes is not within the scope of the present RP. Please also note that the CVMP generally involves stakeholders and academia whenever scientifically useful, and that support and feedback from external experts is always welcome.

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		crucial study design details do not appear to have been considered (or information was not available/reported) in some of the published studies cited in the reflection paper e.g. API, treatment formulation type, treatment group information (replication, animal weight, hair type etc), SPC compliance etc, which makes it difficult to interpret the sources and exposure data. Whilst it is acknowledged that there isn't an average cat or dog, if meaningful interpretation of additional monitoring data is to be achieved, then the nature of the exposure needs to be clearly defined. If a new monitoring programme is to be instigated by CVMP to assess whether further regulation of companion animal parasiticides is warranted, adequate scrutiny of design protocols is essential. Industry would be pleased to participate in such a review and provide feedback on any monitoring proposals. **Proposed change:** Please consider adding text to ensure that stakeholders are involved in the scrutiny of any EMA-funded environmental monitoring programmes.	
1463–1464	10	**Comment:** A study comparing ectoparasiticides levels in faeces and urine from treated dogs would also be useful as part of this research to truly understand the potential impact.	Partly accepted. The wording has been adapted accordingly.
1578–1580	10	**Comment:** Please correct the reference.	Accepted.

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		Proposed change: Diepens, N.J., Belgers, D., Buijse, L. and Roessink, I. (2023) ~~'Science of the Total Environment~~ Pet dogs transfer veterinary medicines to the environment', *Science of the Total Environment*, 858(October 2022), p. 159550. doi:10.1016/j.scitotenv.2022.159550.	The reference has been corrected as proposed.
1679–1680	10	**Comment:** Please correct the reference. **Proposed change:** EMA/CVMP (2022) 'EPAR Exzolt', *[online]*. Available at: ~~https://www.ema.europa.eu/en/medicines/veterinary/EPAR/exzolt~~ **https://www.ema.europa.eu/en/documents/assessment-report/exzolt-epar-public-assessment-report_en.pdf** (Accessed: 30 March 2022).	Not accepted. The referenced document is available under the specified address.
1745–1746	10	**Comment:** Link provided doesn't work. **Proposed change:** Please provide correct link.	Accepted. The link has been corrected.
1896	10	**Comment:** In Table 8, deltamethrin should be written in bold font according to content of Table 4. **Proposed change:** Deltamethrin to be written in bold font.	Accepted. The formatting has been corrected as proposed.
1969–1970	10	**Comment:** *"In some European countries, imidacloprid is still available in pour-on products used for livestock"*	Accepted. Thank you for the comment. Reference to the use as pour-on product has been deleted.

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		Proposed change: Please double check this information confirm. We are not aware of any imidacloprid registrations for livestock.	
1970–1974	10	**Comment:** The Commission Implementing Regulations which finally prohibited imidacloprid in PPPs for outdoor uses were based on EFSA's risk assessment for bee groups (honeybees, bumblebees and solitary bees). "A high risk was concluded for mentioned bee groups or it was concluded that a low risk was not demonstrated." Impact on water organism, earthworm, soil organism... was not considered for the ban and should therefore be omitted here too. **Proposed change:** Please replace sentence starting with "However, based on ..." with "**Due to the conclusion of EFSA on high risk to pollinators, Commission prohibited all outdoor uses of plant protection products containing imidacloprid.**" and please keep references (14/15).	Partly accepted. The mentioned paragraph has been revised, including the proposed sentence.
1979–1980	8	**Comment:** Relating to the use in biocidal products the active substance imidacloprid is approved for non-professional users and for outdoor use (around buildings) as well (at least in Germany). **Proposed change** (if any):	Partly accepted. The term 'professional (use)' has been deleted. Please note that no reference to indoor or outdoor use is given.
2063	8	**Comment**: According to the discussions in the ECHA PBT Expert Group in 2019 permethrin was confirmed to fulfil the P criterion. The active substance fulfils two	Partly accepted.

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		out of three PBT criteria and has therefore to be considered as candidate for substitution in the biocides framework. **Proposed change**: Permethrin is a candidate for substitution under the biocidal regulation.	The proposed change has been added referring to the conclusions of the Biocidal Products Committee (BPC) October 2021 meeting.
2071–2075	8	**Comment**: This section may be updated. In the current draft of the Directive on EQS (Directive 2008/105/EC amended by 2013/39/EU) imidacloprid, deltamethrin and permethrin are listed as priority substances ion Annex I. **Proposed change**: Update of the section according to current draft of Directive on EQS.	Partly accepted. Reference to the EC proposal has been added, however, with reference to the relevant information in Annex V.
2125–2127	10	**Comment:** The sentence is incorrect as studies on environmental effects or fate have been conducted for fluralaner in the course of the authorisation of a VMP indicated for the treatment of the red mite (*Dermanyssus gallinae*) in poultry. EMA CVMP concluded that no risk to the environment is to be anticipated for this use of fluralaner (EMA CVMP "EPAR for Exzolt", cited in the reflection paper as EMA/CVMP (2022)). This information needs to be added. **Proposed change:** As these substances are not authorised as biocides or PPPs, and due to regulatory framework currently in place, no studies on environmental effects or fate have been conducted in the frame of the authorisation procedures of the	Partly accepted. Please note that the sentence: "[…] no studies on environmental effects or fate have been conducted in the frame of the authorisation procedures of the above-mentioned pet VMPs". However, some details on the authorisation of fluralaner as VMP for food-producing animals have been added for more clarity.

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		above-mentioned pet VMPs. **The exception is fluralaner for which studies on environmental effects and fate have been conducted in the course of the authorisation of a VMP indicated for the treatment of the red mite (*Dermanyssus gallinae*) in poultry. EMA CVMP concluded that no risk to the environment is to be anticipated for this use of fluralaner (EMA/CVMP 2022).**	
2132–2133	10	**Comment:** The PNEC surface waters (or hazard limit) for fluralaner is incorrectly presented with 0.00047 µg/L (0.47 ng/L) by Lahr et al. (2019). Lahr et al. (2019) is a secondary reference only as it refers to the "dossier data" as source for the PNEC for surface waters. Obviously, Lahr et al. (2019) made a typing error when transcribing the PNEC from the "dossier data", i.e., the EMA CVMP "EPAR for Exzolt", cited in the reflection paper as EMA/CVMP (2022) (https://www.ema.europa.eu/en/documents/assessment-report/exzolt-epar-public-assessment-report_en.pdf) into their report (in contrast to the PNECs for soil and sediment which were transcribed correctly). It would be preferable for the reflection paper to refer to primary data sources only (in this case the EMA CVMP "EPAR for Exzolt") and to avoid the inclusion of secondary data sources to prevent presentation of incorrect values. The correct value for the PNEC (or hazard limit) is provided in the EMA CVMP "EPAR for Exzolt" with 4.7 ng/L (0.0047 µg/L).	Accepted. The text has been amended as proposed.

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		The conclusion presented in lines 2132-2133 therefore needs to be corrected. **Proposed change:** For fluralaner, ~~Lahr et al. (2019)~~ **EMA/CVMP (2022)** defined a hazard limit of **4.7** ng/L for surface waters based on a chronic NOEC of 47 ng/L in *Daphnia magna*.	
2177	8	**Comment:** The active substance pyriproxyfen is approved for non-professional users (private households) as well (at least in Germany). **Proposed change** (if any):	Accepted. The paragraph has been amended accordingly.
2192	8	**Comment:** The approval of fenoxycarb as active substance in biocidal products has expired. Therefore, the substance is no longer allowed for the use in biocidal products. **Proposed change** (if any):	Accepted. The paragraph has been amended accordingly.