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4 Concept paper for the development of a reflection paper 5 on the environmental risk assessment for parasiticide 6 veterinary medicinal products used in companion animals

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End of consultation (deadline for comments)	31 October 2020

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1. Introduction

In the EU, the environmental risk assessment for veterinary products (VMPs) is tier-based and conducted in two tiers (Phase I and Phase II), in line with VICH guideline 6 (GL 6, EMA 2000) and 38 (GL 38, EMA 2005) for Phase I and Phase II, respectively.

Products for which the environmental risk assessment is concluded in Phase I are those for which the environmental emissions resulting from their use are considered to be negligible and, therefore, their exposure level in the environment is not expected to cause a risk to non-target organisms.

The Phase I guideline (GL 6) makes use of a decision tree to determine if the VMP fulfills the criteria for a higher tier assessment (Phase II) or if the risk assessment can end at Phase I. The environmental risk assessment for products used in companion animals always ends at Phase I, as the decision tree concludes that the use of products for companion animals does not lead to environmental risks, as environmental exposure from their use is assumed to be low. Furthermore, a Phase I assessment for veterinary products used in companion animals does not require information on fate, behaviour and effect data as the overall conclusion is based on exposure considerations only.

Recent scientific publications (e.g., Little and Boxall 2020), however, recommend the need to revisit the assumptions agreed upon during the development of the decision tree used in GL 6, which came into force in July 2000, i.e., that exposure from parasiticide veterinary medicinal products used in companion animals can be considered negligible in the scope of the current environmental risk assessment framework. Hence, these publications challenge the conclusion that environmental risk associated with these products is always neglible, and are calling for a review of the current blanket exclusion of a higher-tier risk assessment for all of these products.

This concept paper has been prepared with the aim to develop a reflection paper, on whether the current approach for the environmental risk assessment of VMPs containing parasiticides, that are used in companion animals remains scientifically justified. The reflection paper will also aim to explore the need and feasibility of mitigation measures for such products.

2. Problem statement

The environmental risk assessment for a veterinary medicinal product can stop in Phase I if it will be used only in companion animals. This provision is reflected specifically in question 3 in the VICH GL 6 (EMA 2000):

VICH GL 6 - *Question 3: Will the VMP be used only in non-food animals?*

Answer: Generally, non-food animals are not intensively reared. Also, product used in these animals are usually individual treatments. Approval of VMPs for use in non-food animal is likely to be associated with fewer environmental concern than approval of VMPs in food producing animals simply because there is less amount of product used.

Despite the above, the CVMP GL in support of VICH GL 6 and GL 38 (EMA 2008) already considered that for ectoparasiticides applied topically to dogs a specific risk mitigation measure, as outlined in the SPC guideline (Guideline on the Summary of Product Characteristics Pharmaceutical Veterinary Medicinal Products, NTA, Volume 6C, section 4.5.*iii*), should be applied to the product information as a standard statement. The recommended risk mitigation measure to be included in the SPC is the following:

"Do not allow treated animals to swim in water courses until at least 2 days after administration".

The omission of this statement would only be considered acceptable where appropriate data are provided to demonstrate absence of a risk to the aquatic compartment.

Termination of the assessment in Phase I is considered acceptable as exposure from the use of companion animal products was considered to be negligible when VICH GL 6 was developed. However, recently published reports indicate that the risk due to exposure from certain substances used in VMPs in companion animals might not be as low as anticipated when this guideline was developed. This is exemplified for parasiticides in particular, given that these are highly toxic to non-target species. Reasons for a possible increase in environmental exposure to parasiticides might include:

1. The treatment of companion animals in the EU with parasiticides has increased

2. The number of companion animals in the EU has also increased

Hence, the assumption that risks associated with exposure to parasiticides can be considered negligible might no longer be valid. In addition, new information has become available on the presence of parasiticides in wastewater treatment plant effluent (Teerlink et *al.* 2017), and on the toxicity of these compounds to aquatic organisms, with extremely low predicted no-effect concentrations (PNECs).

3. Discussion

Since 2000, when VICH GL 6 came into force, applicants and regulators have accepted that risks due to environmental exposure to active substances from products used in companion animals will be low. However, recent publications on the environmental effects of certain parasiticides used in dogs as well as environmental monitoring data (Sadaria et *al*., 2017; Cryder et *al*., 2019), suggest that this situation might have changed since the guideline was developed, and came into force in 2000. Indeed, not only the number of companion animals (i.e., dogs and cats in urban areas) is reported to have increased (over 140 million in the EU (FEDIA 2018)), but also the use of certain ectoparasiticides in companion animals and the pattern of use is reported to be higher (Curtis et *al*., 2016). Thus, the combination of a larger number of treated animals, together with an increased pattern of use might be leading to an increase in the overall environmental exposure for some type of substances, in target compartments. Hence, the resulting environmental exposure may be higher than that which was estimated in 2000, and that could potentially be above established environmentally safe levels (i.e. PNECs).

Effect data show that some of these substances are very toxic to certain organisms. Indeed, it is well reported that most parasiticides are very toxic to insects and crustaceans, and a number can also be considerably persistent in the environment. EFSA reports that the PNECs for certain parasiticides (e.g., imidacloprid and fipronil) are in the ng/l range (EFSA 2013, 2014). These substances have also been reported in wastewater treatment plant effluents (Teerlink et *al*. 2017), and other water systems. While it is not possible, at this time, to establish their source as there may also be other uses for some of these substances, a number of experts consider that the exposure values reported in wastewater cannot be solely explained by their use as plant protection products or biocides. Indeed, initial calculations of exposure concentrations in surface waters from the treatment of dogs with fipronil in the Netherlands, showed that the PNEC for this particular substance would be exceeded if only 10% of the applied dose was washed off in 1% of treated dogs (STOWA 2019). A recent publication has also estimated that the use of neonicotinoid ectoparasiticides in dogs can have a significant impact on the invertebrate wildlife as a result of treated dogs swimming in natural bodies of water (e.g., lake or pond), and potential immediate consequences to its food web (Little and Boxall, 2020). Another report has highlighted a potential link between the death of songbird chicks and the treatment of dogs with parasiticides. An increased mortality might be connected to the exposure resulting from direct contact

of the chick's skin with insecticides accumulated in the hair from dogs treated with parasiticides (hair that parent birds had collected to construct the nests) (Guldemond et *al*., 2019).

The purpose of a future reflection paper would be to research and reflect on the state of knowledge on the emission into the environment of veterinary medicines containing parasiticides that are used in companion animals and on measured and modelled concentrations. The paper would address the potential risks for the environment due to the use of veterinary medicines used in companion animals, reflect on the current assumptions for exposure pathways and overall environmental exposure considerations, also exploring the need and feasibility of mitigation measures. It will also consider whether the current VICH evaluation framework remains appropriate for all type of products used in companion animals, and reflect on possible monitoring options that could be considered for relevant substances (e.g., those that are used under more than one regulatory framework, for instance VMPs and plant protection products) .

4. Recommendation

The CVMP's Environmental Risk Assessment Working Party should reflect on the way in which use of VMPs for companion animals has evolved since introduction of the current framework for the environmental risk assessment and on effect data that have become available for parasiticides and, in this context, consider the strengths and weaknesses of the current framework. Consideration should also be given to the impact that possible risk mitigation measures might have.

5. Proposed timetable

April 2020 – adoption of concept paper for release for consultation by the CVMP

October 2020 – end of consultation period

Timelines for development of the reflection paper will be determined following review of comments received on the concept paper.

6. Resource requirements for preparation

The reflection paper will involve the CVMP ERAWP, ERAWP secretariat and the CVMP. The ERAWP should appoint a rapporteur from amongst its members.

7. Impact assessment (anticipated)

The intended reflection paper will provide an opportunity for the CVMP to reflect on this developing area and for stakeholders to feed into those reflections. The outcome will not change current regulatory requirements, but will help to inform the CVMP of the ongoing appropriateness of those requirements.

8. Interested parties

Pharmaceutical industry, EU national competent authorities, national environmental protection agencies, consultants, contract laboratories

9. References

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