EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 October 2021
EMA/CVMP/ERA/245311/2021
Committee for Medicinal Products for Veterinary Use (CVMP)

Reflection paper on the interpretation of Article 72 of Regulation (EU) 2019/6 — Environmental safety documentation and environmental risk assessment of certain veterinary medicinal products

Draft

Draft agreed by ERAWP	August 2021
Adopted by CVMP for release for consultation	7 October 2021
Start of public consultation	15 October 2021
End of consultation (deadline for comments)	31 January 2022

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Keywords	**Environmental risk assessment, generic veterinary medicinal product, SPC harmonisation**

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Reflection paper on the interpretation of Article 72 of Regulation (EU) 2019/6 — Environmental safety documentation and environmental risk assessment of certain veterinary medicinal products

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1. Introduction

Regulation (EU) 2019/6[1] (VMP-Reg) on veterinary medicinal products (VMPs) shall apply from 28 January 2022, with, amongst others, the following objectives: reducing the administrative burden, enhancing the functioning of the internal market, increasing availability of VMPs as well as safeguarding public and animal health, animal welfare and the environment.

With the specific objective of facilitating the circulation of VMPs within the Union, a new procedure, the so-called "summary of product characteristics (SPC) harmonisation procedure", was created as per Chapter IV, Section 4 ("Harmonisation of the summaries of product characteristics for nationally authorised products") of the aforementioned regulation. As outlined in recital 51 of the VMP-Reg, this procedure aims at aligning the SPCs of nationally authorised VMPs "[...] at least in regard to dosage, use and warnings [...]", in order to reduce "[...] unnecessary barriers for the circulation of VMPs within the Union".

The SPC harmonisation procedure for VMPs can be divided into several phases, including:

1. a selection phase,

2A. an examination phase for the reference VMP (RVMP),

2B. a national phase for updating the SPC of the RVMP,

3A. the harmonisation of the SPCs of generic and hybrid VMPs, and

3B. a national phase for updating the SPCs of the generic and hybrid VMPs.

National competent authorities (NCAs) as well as marketing authorisation holders (MAHs) may propose SPCs of RVMPs for harmonisation for which a marketing authorisation has been granted nationally.

According to Article 70(1) of the VMP-Reg, a list of RVMPs to be subject to SPC harmonisation will be drawn up annually, while , according to Article 72 of the VMP-Reg, "[t]he list referred to in Article 70(1) shall not contain any reference veterinary medicinal product authorised before 1 October 2005 and which is identified as potentially harmful to the environment and has not been subject to an environmental risk assessment. Where the reference veterinary medicinal product is authorised before 1 October 2005 and is identified as potentially harmful to the environment and has not been subject to an environmental risk assessment, the competent authority shall request the marketing authorisation holder to update the relevant environmental safety documentation referred to in point (b) of Article 8(1), taking into account the review referred to in Article 156, and, if applicable, the environmental risk assessment of generic veterinary medicinal products of such reference medicinal products".

To efficiently implement the SPC harmonisation procedure, the Coordination Group for Mutual Recognition and Decentralised Procedures — Veterinary (CMDv) published three best practice guides (BPGs; https://www.hma.eu/631.html#c6783). The present reflection paper aims at complementing the BPGs regarding Article 72 of the VMP-Reg.

[1] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. OJ L 4, 7.1.2019, p. 43–167.

The "BPG for the selection of the products for the SPC harmonisation" (EMA/CMDv/17064/2021) identified certain categories of products which are deemed out of scope of Article 72 of the VMP-Reg. These include: immunological VMPs, VMPs authorised for companion animals only and RVMPs for which a generic has been authorised with the same target species, same indications, same pharmaceutical form, same posology and for which an ecotoxicity evaluation has been performed during the marketing authorisation procedure of the generic.

The following environmental risk assessment (ERA)-related items are particularly relevant in the frame of the implementation of the SPC harmonisation procedure and will be discussed in more detail in this reflection paper:

- RVMPs subject to harmonisation: the list of RVMPs subject to harmonisation will only include RVMPs that have been authorised after 1 October 2005 or RVMPs authorised before 1 October 2005 that are not potentially harmful to the environment.
- ERA for RVMPs falling within the scope of Article 72.
- Environmental warnings to be used within the SPC harmonisation procedure.

To ensure consistent implementation, an approach for classifying an RVMP as "potentially harmful to the environment" in accordance with the second paragraph of Article 72 of the VMP-Reg needs to be defined. Additionally, NCAs and MAHs will benefit from having recommendations on harmonised approaches used for the evaluation of environmental issues (i.e. in the event that the environmental safety documentation requires updating before the SPC harmonisation of a given veterinary product can commence) and for the harmonisation of SPC information with environmental relevance.

In the framework of CMDv's activities regarding harmonisation of the summaries of product characteristics for nationally authorised products CMDv requested CVMP's considerations with regard to implementation of Article 72 of the VMP-Reg. Upon the above-mentioned request and to support CMDv's work within the EU regulatory network, CVMP has provided this reflection paper proposing—for CMDv's consideration—the approach to identify RVMPs which are potentially harmful to the environment in accordance with the second paragraph of Article 72 of the VMP-Reg as well as to harmonise information of environmental relevance within the SPC harmonisation procedure, and providing advice on the conduct of an ERA for RVMPs that have been authorised before 1 October 2005 and identified as potentially harmful to the environment.

Thus, the scope and aims of the present reflection paper can be defined as follows: (i) to propose an approach for the identification of RVMPs which are potentially harmful to the environment in accordance with the second paragraph of Article 72 of the VMP-Reg; (ii) to provide advice on the conduct of an ERA for RVMPs that have been authorised before 1 October 2005 and identified as potentially harmful to the environment; and (iii) to consider an approach(es) to harmonise information of environmental relevance within the SPC harmonisation procedure.

2. Discussion

The present reflection paper aims at addressing specific ERA-related issues relevant to the following three processes (sections 2.1–2.3) associated with Article 72 of the VMP-Reg, and which are also detailed in **Figure 1**:

- **Section 2.1** (questions Q1–Q3; blue-coloured boxes) discusses the approach to classify RVMPs potentially harmful to the environment in accordance with Article 72 of the VMP-Reg.
- **Section 2.2** (red-coloured box) provides recommendations on on the conduct of an ERA for RVMPs that will be identified as those falling under Article 72 of the VMP-Reg.
- **Section 2.3** (orange-coloured boxes) reflects on ERA-related issues potentially arising within the frame of the SPC harmonisation procedure for relevant RVMPs and their generics.

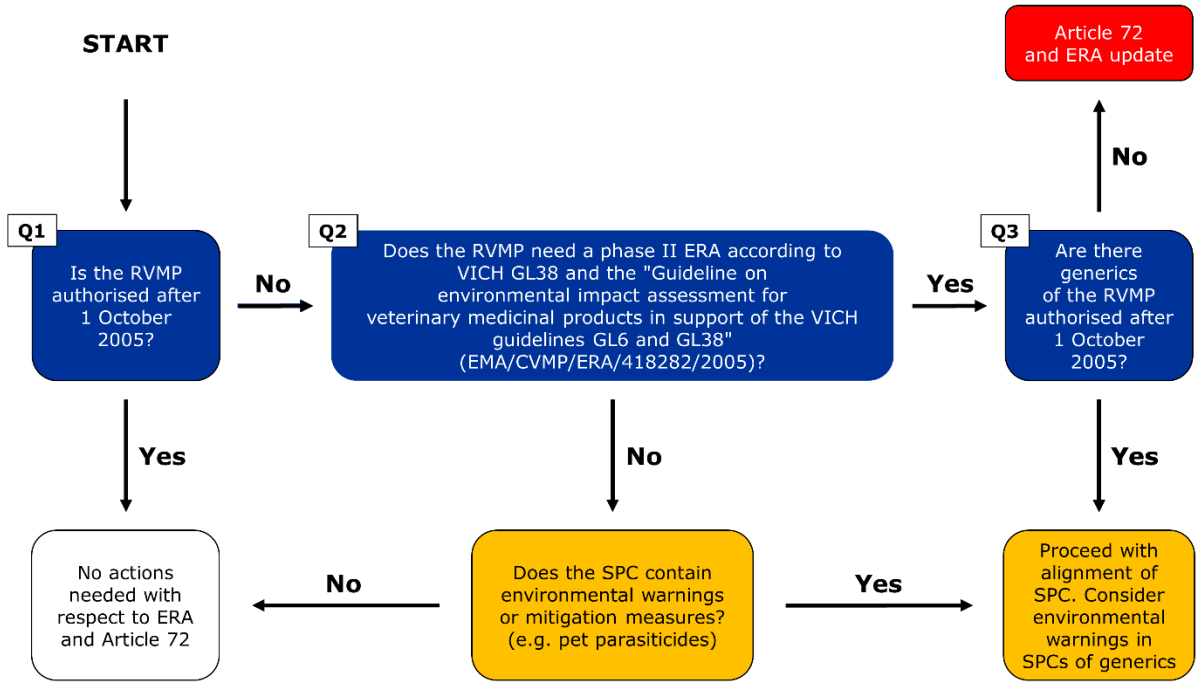

Figure 1: Graphical representation of the approach proposed within the present reflection paper for the interpretation of Article 72 of the VMP-Reg.

2.1. Approch to classifying RVMPs as potentially harmful to the environment

It is acknowledged that the term "potentially harmful to the environment" used in the second paragraph of Article 72 of the VMP-Reg may be subject to broad interpretation and meanings in different contexts and legislative frameworks. For this reason, the meaning(s) of this term is/are not exhaustively discussed in the present document.

To identify whether an RVMP falls under the Article 72 of the VMP-Reg and an update of the ERA information is needed, three questions (Q1–Q3; also outlined in **Figure 1**) should be addressed for each RVMP of concern. Corresponding criteria and decisions are supported by existing regulatory principles and documents as indicated in the text below.

The following types of RVMPs are considered as <u>not falling within the scope of Article 72 of the VMP-Reg:</u>

- Q1: **RVMPs authorised after 1 October 2005**, as specifically mentioned in Article 72 of the VMP-Reg.
- Q2: **RVMPs authorised before 1 October 2005 for which the ERA ends in phase I** in accordance with VICH GL6 ("Environmental impact assessment [EIAS] for veterinary medicinal products — Phase I" [CVMP/VICH/592/98-FINAL]) and the relevant section of the "Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38" (EMA/CVMP/ERA/418282/2005), i.e. VMPs with an environmental exposure below trigger values not posing a concern as well as VMPs exempted by VICH GL6 such as products containing active substances of biological or natural origin or VMPs solely intended for non-food-producing animals.
- Q3: **RVMPs authorised before 1 October 2005 for which a phase II ERA is indicated but for which a generic has been authorised after 2005** as this situation would imply that the environmental information has already been made available to some NCA in the EU/EEA.

The three principles and selection criteria outlined in Q1, Q2 and Q3 directly correspond to the criteria defined by the CMDv in its "BPG for the selection of the products for the SPC harmonisation" (EMA/CMDv/17064/2021).

2.2. ERA for RVMPs falling within the scope of Article 72

RVMPs that fall within the scope of Article 72 of the VMP-Reg are those that have been authorised before 1 October 2005, for which an ERA performed according to VICH GL6 indicates a requirement to perfrom a phase II ERA and for which there is no generic authorised in the EU/EEA after 1 October 2005.

Before harmonising SPCs of these RVMPs, an ERA should be performed as required by VICH GL38 as well as the "Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38" (EMA/CVMP/ERA/418282/2005), and the outcome of this ERA (in the form of environmental safety information or risk mitigation measures) would then be used during the SPC harmonisation procedure.

In case a monograph or alternate system according to Article 156 of the VMP-Reg will be available in the future, this information should be taken into account for the update of the ERA as suggested by the Article 72.

2.3. Environmental issues in the frame of the SPC harmonisation procedure

For RVMPs identified as not falling within the scope of Article 72 of the VMP-Reg, information contained within the SPC is expected to be harmonised.

It is recommended to apply the following general principles:

- Harmonisation of environmental warnings may also encompass products not directly falling under Article 72 according to the CMDv "BPG for the selection of the products for the SPC harmonisation" (EMA/CMDv/17064/2021), e.g. VMPs for companion animals, and relevant environmental warnings and risk mitigation measures should be considered and used during the SPC harmonisation procedure (see also orange-coloured box in **Figure 1**).

- In the case where the SPC(s) of (a) generic VMP(s) contain(s) information regarding environmental issues, mutual trust between NCAs should be applied, i.e. where one or several NCAs have assessed an ERA for a generic VMP while other NCAs have not, all NCAs should rely on the outcome of the existing assessment(s).
- Any measures to mitigate the risk to the environment or environmental information or disposal advice applied to the generic product should also be applied to its reference product.
- Generics/hybrids authorised for a subset of target species/indications with the aim to avoid a phase II ecotoxicity assessment will only be harmonised for the parts of the SPC related to the subset of target species/indications.
- In the case that SPCs of generic products authorised after 1 October 2005 do not contain any specific environment-related information or warnings, then environmental issues do not need to be addressed during the SPC harmonisation procedure for the reference product, i.e. no actions need to be taken.

Several sections of the SPC and the package leaflet listed below are relevant, and the information related to ERA should be aligned based on the outcome of individual ERAs performed for generics in the Member States.

The numbering of the SPC and package leaflet sections given below corresponds to the future veterinary product information template (QRD template version 9.0) developed by the European Medicines Agency's (EMA) Working Group on Quality Review of Documents (QRD) intended to take account of the requirements of Regulation (EU) 2019/6 (https://www.ema.europa.eu/en/veterinary-regulatory/marketing-authorisation/product-information/veterinary-product-information-templates).

It is recommended to use standardised sentences whenever possible as outlined in the QRD template and follow the existing CVMP documents such as those cited in the following paragraphs:

- The sub-section on **"Environmental properties"** within section 4 of the SPC and section 17 of the package leaflet would, for instance, need to be amended if the active substance is classified as persistent or toxic according to the "Guideline on the assessment of persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substances in veterinary medicinal products (EMA/CVMP/ERA/52740/2012).
- The sub-section on **"Special precautions for the protection of the environment"** within section 3.5 of the SPC and section 6 of the package leaflet would need to be amended if (i) **risks are identified for soil or dung fauna**; and/or (ii) if **risks are identified for surface, ground water or sediment.** It is recommended to thereby consider the "Reflection paper on risk mitigation measures related to the environmental risk assessment of veterinary medicinal products" (EMA/CVMP/ERAWP/409328/2010).
- Section 5.5 of the SPC and section 12 of the package leaflet (**"Special precautions for the disposal of unused product or waste materials, if any"**) should be amended if **risks are identified for surface, ground water or sediment** and recommendations on VMP disposal should always be included as given in the QRD template.