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3 Committee for Medicinal Products for Veterinary Use (CVMP)

4 Concept paper for the revision of scientific guidelines on 5 limited market for veterinary medicinal products.

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1. Introduction

With the aim of promoting availability of veterinary medicines, the Agency established in 2009 (revised in 2014) a policy, complemented by supporting guidance, for Minor Uses/Minor Species which defined a procedure for classification of products as MUMS as well as the support provided to companies submitting marketing authorisation applications for veterinary medicinal products that have been classified as MUMS/Limited markets. This support includes financial incentives (fee waivers and fee reductions) and reduced data requirements.

The CVMP developed specific guidelines detailing reduced data requirements for products classified as MUMS in relation to quality, efficacy and safety of pharmaceutical veterinary medicinal products also in relation to immunological veterinary medicinal products. The guidelines were initially developed in 2006 and 2007 and subsequently revised in 2016.

The Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products (repealing Directive 2001/82/EC) entered into force on 28 January 2019 and is applicable from 28 January 2022 onwards. The Regulation introduces specific provisions for limited markets, including a definition, the procedure for granting marketing authorisations, and their renewal.

In the preamble of the Regulation (recital 30) it is acknowledged that companies have less interest in developing veterinary medicinal products for markets of a limited size. The recital also states that: '*In order to promote the availability of veterinary medicinal products within the Union for those markets, in some cases it should be possible to grant marketing authorisations without a complete application dossier having been submitted, on the basis of a benefit-risk assessment of the situation and, where necessary, subject to specific obligations. In particular, the grant of such marketing authorisations should be possible in the case of veterinary medicinal products for use in minor species or for the treatment or prevention of diseases that occur infrequently or in limited geographical areas*.'

2. Problem statement

The current guidelines were developed with the aim of reducing data requirements, where possible, for products classified as MUMS/Limited markets, according to the Agency's policy, while still providing assurance of appropriate quality, safety, and efficacy, and complying with the legislation in place, leading to an overall positive benefit-risk balance for the product.

Regulation (EU) 2019/6 introduces a specific legal basis for veterinary medicinal products intended for limited markets as outlined below.

- **Article 4 (29b)** defines 'limited markets' as follows:

  '*Limited market means a market for one of the following medicinal product types:*

  - *(a) veterinary medicinal products for the treatment or prevention of diseases that occur infrequently or in limited geographical areas;*
  - *(b) veterinary medicinal products for animal species other than cattle, sheep for meat production, pigs, chickens, dogs and cats;*

The definition considers veterinary medicinal products intended for Atlantic salmon as falling under the provisions that can be subject to limited market while the current CVMP guidelines consider Atlantic salmon a major species.

- **Article 23** introduces a derogation in relation to data requirements for applications for limited markets as follows:

  1. By way of derogation from point (b) of Article 8(1), the applicant shall not be required to provide the comprehensive safety or efficacy documentation required in accordance with Annex II, if all of the following conditions are met:

  (a) the benefit of the availability on the market of the veterinary medicinal product to the animal or public health outweighs the risk inherent in the fact that certain documentation has not been provided;

  (b) the applicant provides the evidence that the veterinary medicinal product is intended for a limited market.

- **Article 24** introduces the validity of a marketing authorisation for a limited market as follows:

  1. By way of derogation from Article 5(2), a marketing authorisation for a limited market shall be valid for a period of 5 years.

  2. Before the expiry of the five-year period referred to in paragraph 1 of this Article, marketing authorisations for a limited market granted in accordance with Article 23 shall be re-examined on the basis of an application from the holder of that marketing authorisation. That application shall include an update benefit-risk assessment

In preparation for the implementation Regulation (EU) 2019/6, the existing MUMS/limited markets guidelines should be revisited and updated in line with the new legal provisions including consideration of data requirements for biological veterinary medicinal products other than immunologicals, not covered by the existing guidelines.

In addition to the revision the guidelines, the CVMP will also consider criteria for eligibility for limited markets in view of the new provisions in the Regulation. This work will be developed in parallel with the revision of the guidelines, but it is outside of the scope of this concept paper.

3. Discussion

The revision of the guideline will consider the new legal basis and definitions of Regulation (EU) 2019/6 and will reflect on the experience gained with the evaluation of MUMS/Limited markets applications.

The following specific aspects will be discussed and covered as appropriate in revision of the concerned guidelines:

3.1 Safety and residue data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMEA/CVMP/SWP/66781/2005-Rev.1)

The reduced data requirements detailed in the current guideline are considered in principle appropriate in relation to consumer safety and user safety.

In relation to environmental risk assessment (ERA), a discussion is foreseen on whether further data reductions are possible.

The review of the guideline will also consider safety and residue data requirements for Atlantic salmon, now included in the definition of 'Limited market' under Regulation (EU) 2019/6, while previously considered a major species when the current guidelines were developed and therefore not considered by the MUMS policy.

3.2 Efficacy and target animal safety data requirements for veterinary medicinal products intended for minor uses or minor species (EMEA/CVMP/EWP/117899/2004-Rev.1)

Regulation (EU) 2019/6 foresees that applications for marketing authorisations for products meeting the conditions of limited markets are not required to provide comprehensive efficacy data. Marketing authorisations granted under these circumstances are valid for 5 years but can become definitive provided that data in line with the requirements of Annex II of the Regulation are submitted. Considering the new legal provisions, the revision of the guideline will aim at establishing the minimum data package required for assessing efficacy and in particular addressing the concepts of 'proof of efficacy' or 'proof of concept' (noting that Article 37(2g) of Regulation (EU) 2019/6 indicates that a marketing authorisation shall be refused if…….*"the applicant has not provided sufficient proof of efficacy as regards the target species*").

The review of the guideline will also consider efficacy and target animal safety data requirements for Atlantic salmon, now included in the definition of 'Limited market' under Regulation (EU) 2019/6, while previously considered a major species when the current guidelines were developed and therefore not considered by the MUMS policy.

3.3 Data requirements for immunological veterinary medicinal products intended for minor use or minor species (EMEA/CVMP/IWP/123243/2006 Rev. 3)

Regulation (EU) 2019/6 introduces the definition of biologicals and in the context of the advice provided to the European Commission on the revision of Annex II (EMA/CVMP/351417/2019) the CVMP recommended specific data requirements for biological veterinary medicinal products, including data requirements for immunologicals.

The review of the guideline will also consider data requirements for Atlantic salmon, now included in the definition of 'Limited market' under Regulation (EU) 2019/6, while previously considered a major species when the current guidelines were developed and therefore not considered by the MUMS policy.

4. Recommendation

CVMP recommends the revision of the following guidelines:

- Safety and residue data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMEA/CVMP/SWP/66781/2005- Rev.1)
- Efficacy and target animal safety data requirements for veterinary medicinal products intended for minor uses or minor species (EMEA/CVMP/EWP/117899/2004-Rev.1)
- Data requirements for immunological veterinary medicinal products intended for minor use or minor species (EMEA/CVMP/IWP/123243/2006 Rev.3)

The review is required in advance of the applicability of the Regulation in order to allow applicants to prepare and submit applications for veterinary medicinal products for limited markets according to the new legal framework from January 2022.

It is noted that the derogation concerning data requirements for limited market applications in Regulation (EU) 2019/6 does not include quality data and as a consequence there is no legal basis for reduced data requirements on quality. Therefore, the existing guideline on quality data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMEA/CVMP/QWP/128710/2004-Rev.1) will be withdrawn and the existing guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species

(EMEA/CVMP/IWP/123243/2006 Rev. 3) will be revised accordingly to delete any reference to quality data.

5. Proposed timetable

31 January 2020: Deadline for comments from stakeholders

June 2020: Expected date for CVMP adoption of the revised guidelines for release for consultation

September 2020: Expected end of consultation

January 2021: Expected publication of revised guidelines

6. Resource requirements for preparation

Expertise of the CVMP and relevant working parties on the different relevant areas will be required with 3 drafting groups (1 per guideline) of 4-5 members being constituted. It is expected that over the total of 10 months required for the work (see timetable above) the groups could meet virtually once a month and members of the groups will contribute to the drafting of the guidelines in between.

7. Impact assessment

The update of these guidelines is expected to provide clearer and up-to-date guidance to applicants and assessors in relation to applications to be submitted under the new legal provisions ensuring alignment of the guidelines with the new Regulation.

Overall it is anticipated that the revised guidelines will have a positive impact on the development of applications for the treatment or prevention of diseases that occur infrequently or in limited geographical areas and therefore promoting availability of veterinary medicines for limited markets.

8. Interested parties

Veterinary pharmaceutical industry and consultants, EU Regulatory authorities.

9. References to literature, guidelines, etc.

- Directive 2001/82/EC of the European Parliament and the Council of 6 November 2001 on the Community Code relating to Veterinary Medicinal Products as amended.
- 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.