EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 October 2021
EMA/CVMP/435071/2021
Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on scientific guidelines for limited market products deemed not eligible for authorisation under Article 23 of Regulation 2019/6

Draft

Adopted by CVMP for release for consultation	7 October 2021
Start of public consultation	15 October 2021
End of consultation (deadline for comments)	15 December 2021

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

Keywords	**Availability, limited market, classification, Article 8, Article 23, eligibility, Regulation (EU) 2019/6, veterinary medicinal products**

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1. Introduction

From 28 January 2022, the current EMA policy on MUMS/limited market classification will cease to apply.

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 (Articles 23 and 24).

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*.'

Based on Recital 30, it is understood that the objective of the Article 23 (Applications for limited markets) provision is to promote availability where products may not be brought to the market because of small market size, by making it possible to grant marketing authorisations without a complete application dossier. Where eligibility for consideration in accordance with Article 23 is accepted, the legislation makes it possible to grant marketing authorisations in the absence of certain safety and/or efficacy data required by Annex II (COMMISSION DELEGATED REGULATION (EU) 2021/805 of 8.3.2021 amending Annex II to Regulation (EU) 2019/6 of the European Parliament and of the Council). Notably, Article 23 does not provide for a reduction in requirements for Quality data.

Definitions:

'Limited market' - according to Article 4(29) of Regulation (EU) 2019/6, '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.*"

'Limited market product eligible for Article 23' – a product that meets the definition of limited market and, in addition, it is accepted that *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* (satisfies Article 23(1)(a) of Regulation (EU) 2019/6).

'Limited market product not eligible for Article 23' – a product that meets the definition of limited market, but it is not accepted that *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* (does not satisfy Article 23(1)(a) of Regulation (EU) 2019/6).

2. Problem statement

At the July 2021 CVMP meeting, the following guidance documents on the safety and efficacy requirements for limited market products deemed eligible for consideration under Article 23 were adopted:

- Guideline on data requirements for applications for immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 - (EMA/CVMP/59531/2020)
- Guideline on efficacy and target animal safety data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 - (EMA/CVMP/52665/2020)
- Guideline on safety and residue data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 - (EMA/CVMP/345237/2020)

However, not all products that satisfy criteria to be classified as 'intended for a limited market' are automatically eligible for consideration under Article 23. Additionally, an applicant is required to show that 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 (Article 23(1)(a)).

If a product satisfies the criteria to be classified as a limited market (according to Article 4(29)) but is not considered eligible for consideration under Article 23 then, by default, the application dossier must be submitted under Article 8 of Regulation (EU) 2019/6. For Article 8 applications, which will include applications for limited market products deemed not eligible for authorisation under Article 23, technical documentation necessary for demonstrating the quality, safety and efficacy of the veterinary medicinal product must be in line with the requirements set out in Annex II (Annex II compliant). Currently, there is no guidance on the data requirements for limited market products that are deemed not eligible for authorisation under Article 23.

3. Discussion (on the problem statement)

When considering eligibility for authorisation of products intended for a limited market, there are two questions that have to be addressed. The first of these questions is "is the proposed indication/product for a limited market as defined in Article 4(29) of the Regulation?" (that is, has the applicant provided evidence that the veterinary medicinal product is intended for a limited market as required by Article 23(1)(b)?).

Any product that is not classified as a limited market will automatically default to a full application in accordance with Article 8 (Annex II compliant).

For those products that are classified as limited market, the second question to be addressed in order to be considered eligible for authorisation in accordance with Article 23 is "does the proposed product satisfy the condition detailed in Article 23(1)(a)?". The approaches to classifying a product as intended for a limited market and for determining if the "*benefit of 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*" are outlined in the CVMP reflection paper on classification of a

product as intended for a limited market according to Article 4(29) and/or eligibility for authorisation according to Article 23 (Applications for limited markets).

Where eligibility for consideration in accordance with Article 23 is accepted, the legislation makes it possible to grant marketing authorisations in the absence of certain safety and/or efficacy data. Guidelines detailing the gaps in pivotal data (relative to Annex II) that may be accepted for a product deemed eligible for consideration in accordance with Article 23 have been adopted by the CVMP. Notably, Article 23 does not provide for a reduction in requirements for Quality data.

If a product that is classified as a 'limited market' is not eligible for consideration under Article 23 then, by default, an Annex II compliant dossier will be required. However, one of the objectives of the overall approach to applying the Article 23 provision was to allow for a situation where the regulatory system can continue to encourage/promote development of the type of product that is being authorised currently as a MUMS/limited market product (that is, indications/products intended for limited markets should benefit from this classification even if not considered eligible for Article 23). Noting this objective, therefore, CVMP advised that specific data requirements guidance should be elaborated for indications/products that are classified as a 'limited market' but are not eligible for consideration under Article 23. That is, while there is an obligation that the dossier complies with the requirements of Annex II, it is recognised that there may be some flexibilities possible vis-à-vis data requirements expected for a product not classified as a limited market product (i.e. does not meet the definition of limited market as defined in Art. 4(29)).

With the objective of highlighting appropriate data requirements for such products, it is proposed that the following set of documents should be developed:

- Guideline on quality data requirements for applications for non-biological products intended for limited markets (applicable to applications submitted under either Article 8 or Article 23).
- Guideline on safety and residues data requirements for applications for non-IVMPs intended for limited markets but not deemed eligible for authorisation under Article 23.
- Guideline on efficacy and target animal safety data requirements for applications for non-IVMPs intended for limited markets but not deemed eligible for authorisation under Article 23.
- Guideline on quality data requirements for applications for biological products (including IVMPs) intended for limited markets (applicable to applications submitted under either Article 8 or Article 23).
- Guideline on safety and efficacy data requirements for applications for IVMPs intended for limited markets but not deemed eligible for authorisation under Article 23.

Regarding quality guidance specifically, the intention is to elaborate guidance for quality requirements for limited market products that are Annex II compliant (noting that this is a requirement of the legislation), but highlighting some flexibilities possible vis-à-vis data requirements expected for a product not classified as a limited market product. Such guidance could be applied regardless of the underlying legal basis (that is, Article 8 or Article 23).

4. Recommendation

The CVMP recommends the drafting of the following set of documents:

- Guideline on quality data requirements for applications for non-biological products intended for limited markets (applicable to applications submitted under either Article 8 or Article 23).

- Guideline on safety and residues data requirements for applications for non-IVMPs intended for limited markets but not deemed eligible for authorisation under Article 23.
- Guideline on efficacy and target animal safety data requirements for applications for non-IVMPs intended for limited markets but not deemed eligible for authorisation under Article 23.
- Guideline on quality data requirements for applications for biological products (including IVMPs) intended for limited markets (applicable to applications submitted under either Article 8 or Article 23).
- Guideline on safety and efficacy data requirements for applications for IVMPs intended for limited markets but not deemed eligible for authorisation under Article 23.

Stakeholders are invited to comment on the overall recommendation and provide specific comment on what should be addressed and/or provided for in each of the proposed guidance documents, while noting that data requirements will have to satisfy the basic requirements of Annex II of the Regulation.

5. Proposed timetable

January 2022:	Deadline for comments from stakeholders
June 2022:	Expected date for CVMP adoption of the draft guidelines for release for consultation
September 2022:	Expected end of consultation
January 2023:	Expected publication of final guidelines

6. Resource requirements for preparation

Expertise of the EWP-v, IWP, QWP and SWP-v will be required. In addition, it is proposed that an 'oversight' group, including in its membership relevant working party chairs, will be established to actively engage on the elaboration of guidance for limited market products not deemed eligible for Article 23 and coordinate that activity.

It is expected that a total of 12 months will be required for completion of this task.

7. Impact assessment (anticipated)

The guidelines are 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. Where relevant, the documents will help to clarify the differences in data requirements between applications for limited markets eligible for authorisation under Article 23 of Regulation (EU) 2019/6 and those deemed not eligible for authorisation under Article 23.

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.

- 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 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0006&from=EN
- Commission Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 of the European Parliament and of the Council https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R0805&from=EN
- Limited market guidelines adopted by CVMP in July 2021:
  - Guideline on data requirements for applications for immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 - (EMA/CVMP/59531/2020)
  - Guideline on efficacy and target animal safety data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 - (EMA/CVMP/52665/2020)
  - Guideline on safety and residue data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 - (EMA/CVMP/345237/2020)