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MUMS/limited market scheme for veterinary medicinal products

12th Annual Report (01/01/2021 – 31/12/2021)

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Summary

Twelve years ago the European Medicines Agency (the Agency) launched Minor Use Minor Species (MUMS)/limited market initiatives as a part of measures to promote availability of veterinary medicinal products. The aim of the scheme was to facilitate the access to the market for products indicated for use in minor species or for the treatment or prevention of diseases that occur infrequently or in limited geographical areas.

The MUMS/limited market policy for classification and incentives for veterinary medicinal products indicated for Minor Use Minor Species (MUMS)/limited market (EMA/308411/2014) (the policy) [1] was established with the goal to stimulate the development of new veterinary medicinal products for minor species and for rare diseases in major species that would otherwise not be developed in the current market conditions. The policy provided two types of incentives: reduced data requirements and financial incentives by means of fee exemptions or fee reductions.

In those twelve years of application of the scheme, the Committee for Veterinary Medicinal Products (CVMP) successfully reviewed 318 requests for classification as MUMS/limited market either for products indicated for minor species (e.g. rabbits, ducks, guinea pigs, foxes, ferrets, goats, turkeys and bees) or for indications for products to be used in the major species (dogs, cats, chickens, pigs, sheep, salmon and cattle) where the use was considered as minor and the market as limited.

Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products (repealing Directive 2001/82) [2] (VMP Regulation or Regulation (EU) 2019/6)) introduced for the first time the legal basis for granting marketing authorisations for products targeted to limited markets. The policy and complementary guidance were reviewed and considered largely consistent with the conditions and requirements of the VMP Regulation in respect of limited markets. However, on the basis of the new legal provisions laid out in the Regulation (EU) 2019/6), the policy was considered obsolete and ceased to apply on 28 January 2022, that is when the VMP Regulation became applicable.

It is expected that the experience gained during the success story of the MUMS/limited market scheme for veterinary medicinal products, which has brought 29 products to the market through the centralised procedure, will be a valuable tool in promoting the products for limited market by the means of implementation of the specific articles (23 and 24) addressing limited markets in the VMP Regulation.

Background

The Agency implemented the first policy for classification and incentives for veterinary medicinal products indicated for Minor Use Minor Species (MUMS)/limited market on 1 September 2009, which was updated later in July 2013. The revised version of the policy was agreed in December 2014 and further amended in December 2018 (EMA/308411/2014-Rev.1) and in December 2021 when it was extended until 28 January 2022.

The MUMS/limited market initiative represented a joint activity between the Agency and the European Medicines Regulatory Network aiming to facilitate the access to market of products indicated for MUMS/limited market as part of measures to promote the availability of veterinary medicinal products. It is worth noting that activities to promote the availability of veterinary medicinal products continue to be promoted in the European medicines agencies network strategy to 2025 as well as in the corresponding work plans of the Agency and the Heads of Medicines Agencies (HMA).

To date, 11 Annual reports have been provided to EMA Management Board (MB), including a summary on the operation of the MUMS/limited market scheme. The current annual report covers the activities

carried out under the MUMS/limited market scheme during its last year of operation, between 1 January and 31 December 2021.

MUMS/limited market activities in 2021

Classification of products/indications by CVMP in 2021

In the twelfth year of operation of the MUMS/limited market scheme for veterinary medicinal products, (i.e. year 2021) the CVMP reviewed 14 requests for classification as MUMS/limited market, including products indicated for the following minor species: goats, turkeys, fish (sea bream), honey bees, ducks, horses, minks and zoo species. Classification was also sought for minor use/limited market indications for products to be used in the following major species: dogs, cats, fish (salmon), sheep, pigs and cattle.

In this report a distinction is made between the products which were classified for the first time by CVMP as indicated for a MUMS/limited market and the products for which CVMP confirmed that reclassification as MUMS/limited market remained appropriate. Considering that the policy was coming to a closure, all MUMS classification holders were informed that the classifications would cease to be valid on 28 January 2022.

From the total of 14 requests reviewed in 2021, 9 were initial classification requests and 5 were reclassification requests. All 14 requests (100%) were classified as MUMS/limited market.

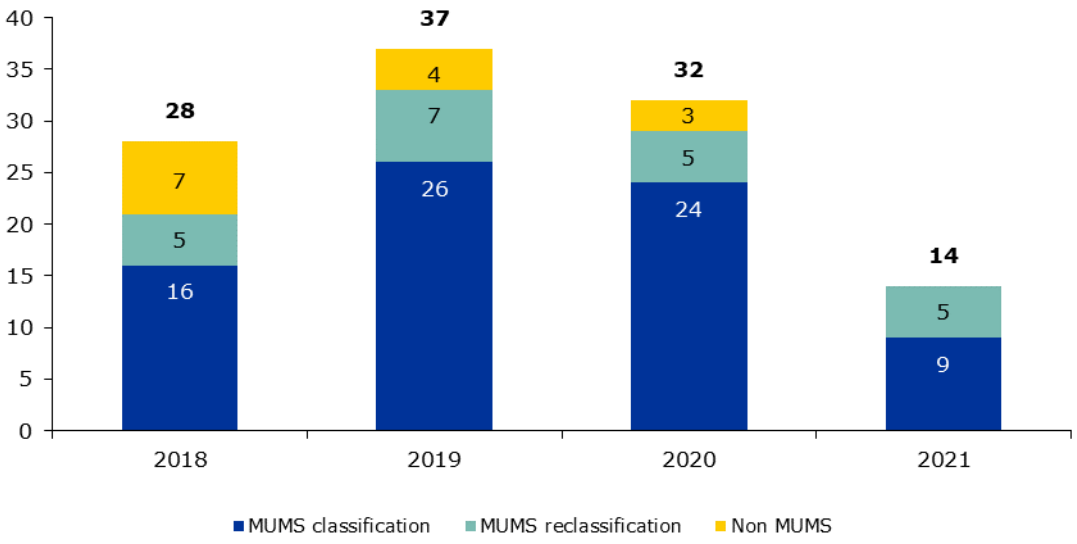
Among the products classified as MUMS/limited market, 6 (43%) were recommended as eligible for financial incentives (there were 21% in 2020), whilst 8 (57%) were not recommended as eligible for financial incentives (there were 79% in 2020), as these were either not indicated for a food producing species and/or an alternative product was authorised for the same indication.

It is worth noting that already at the end of 2021, the CVMP received three requests for classification of a veterinary medicinal product as intended for a limited market according to Article 4(29) and for eligibility for authorisation according to Article 23 of Regulation (EU) 2019/6. The outcome of those requests is not reflected in this report.

Table 1: Outcome of MUMS/limited market (re)classification requests in 2017–2021

MUMS/limited market classification and reclassification					
Year	**2017**	**2018**	**2019**	**2020**	**2021**
MUMS classification					
with financial incentives	3	1	4	5	5
without financial incentives	15	15	22	19	4
MUMS reclassification					
with financial incentives	2	0	1	1	1
without financial incentives	7	5	6	4	4
Not MUMS	2	7	4	3	0
TOTAL	**29**	**28**	**37**	**32**	**14**

Figure 1: Number of requests for (re)classification by CVMP from 2018-2021



Incentives provided as a result of classification in 2021

In 2021, six out of the total of 14 requests (43%) for classification as MUMS/limited market were from companies registered as micro, small and medium-sized enterprises (SMEs) at the Agency. Where appropriate, applicants are encouraged to register as an SME under Commission Regulation (EC) 2049/2005 and to avail of the financial incentives on offer under this scheme in the first instance. Close liaison is maintained between the Agency's Veterinary Medicines Division and SME office to facilitate that applicants requesting MUMS/limited market classification for their products also register as SMEs, whenever appropriate. This approach has shown beneficial results in terms of a general increase in the number of registered SMEs within the veterinary domain.

By the end of 2021, 61 companies working in the veterinary medicinal products field and 78 in both human and veterinary fields were registered as SMEs, representing respectively about 3.5% and 4.5% of the total number of companies registered as SMEs.

Scientific advice requests or letters of intent to request scientific advice were submitted for 5 MUMS/limited market products in 2021.

Applicants applying for authorisation of products under MUMS/limited market are able to refer to **specific reduced data requirements** as in the relevant guidelines which can reduce the need for specific studies. In this context:

- One full new **marketing authorisation application** for MUMS/limited market product was **validated** for the centralised procedure in 2021 and two were validated in January 2022. In total, six applications are currently under assessment.
- Four **centralised marketing authorisations** were granted in 2021 for the following products classified by CVMP as MUMS/limited markets:
  - Fatrovax RHD (a new vaccine for the active immunisation of rabbits from 28 days of age against rabbit haemorrhagic disease caused by RHDV and RHDV2);

- Strangvac (a new vaccine for the active immunisation of horses and ponies to reduce clinical signs of disease and bacterial shedding caused by infection with *Streptococcus equi*).
- Felpreva (an antiparasitic veterinary medicine, containing tigolaner, emodepside and praziquantel, for the treatment of cats that have, or that are at risk from, mixed parasitic infestations/infections)
- NexGard Combo (an antiparasitic veterinary medicine, containing esafoxolaner, eprinomectin and praziquantel, for the treatment of mixed infections with external parasites (fleas, ticks or ear mites) and internal parasites (tapeworm and roundworms) in cats)

The costs of the scheme to the Agency in terms of fees waived or reduced in 2021 was of € 168,300 (€136,232.80 reported in 2020). The restriction of financial incentives to food-producing species was agreed as part of the changes in the policy in 2013 and took full effect in the autumn of 2018. Financially, the effect was visible from 2019.

MUMS/Limited Markets policy, guidance and CVMP guidelines on data requirements

As already stated, the policy, as a part of a joint activity between the Agency and the European Medicines Regulatory Network, aimed to facilitate the access to market of products indicated for MUMS, as part of measures to promote the availability of veterinary medicinal products.

Recognising the limited interest from companies to invest in these types of products and in order to maximise the possibilities for attracting interest in this area, the policy did not restrict consideration of requests for MUMS/limited market classification to companies established in the EU. However, incentives regarding fee reductions on assessment or post-authorisation applied only to those companies established in the EU territory.

The policy was updated in July 2013 to restrict the financial incentives to food producing animals only. The change came into force in September 2013. The policy was further revised in 2018 in order to clarify that fee incentives could only be granted to sponsors /applicants (owners) placed within the EU.

To complement the policy, a guidance document for applicants "Guidance on the classification of veterinary medicinal products indicated for minor use minor species (MUMS) / limited market" (EMA/CVMP/388694/2014) (the guidance) [3], was adopted in December 2014.

The guidance gave directions for implementing the updated policy and described the procedure and the steps to be followed by the applicant and the Agency when dealing with requests for MUMS/limited market classifications.

Further to the revision of the guidelines on data requirements for veterinary medicinal products intended for MUMS/limited market (adopted by CVMP in 2016-2017), the guidance on the classification of veterinary medicinal products for MUMS/limited markets was revised in October 2017. The opportunity was taken to simplify the request process for applicants.

A second revision of the guidance was adopted in 12 December 2018, to align it with the policy clarifying that incentives regarding fee reductions on assessment or post-authorisation would only apply to those companies established in the EU territory.

In order to assist the companies further, the "Q&A - EMA guidance for companies requesting classification for products/indication as Minor Use Minor Species (MUMS)/limited market" (EMA/CVMP/370663/2009) [4] document was created in 2009. It described the practice for processing MUMS/limited market applications and addressed in detail a number of questions that applicants

requesting (re)classification of products/indications for minor use or minor species (MUMS)/ limited market might have had.

EMA's MUMS/limited market policy ceased to apply once Regulation (EU) 2019/6 (VMP Regulation) became applicable on 28 January 2022, as that Regulation contains new legal provisions on veterinary medicinal products intended for limited markets.

Support to applicants for determination of reduction of data requirements

CVMP guidelines on MUMS/limited market data requirements (quality [5], safety [6], efficacy [7] and immunologicals [8]) were in place to assist applicants in the preparation of their dossiers for marketing authorisations. The specific data requirements that applied in the case of MUMS/limited market products or indication in a product were important for industry as they could reduce the number of the studies needed to support a new application, and hence reduce the overall cost for product development. Following the publication of Commission Regulation (EU) 2017/880 on the establishment of maximum residue limits (MRLs), the guideline on safety and residue data requirements for pharmaceutical veterinary medicinal products intended for MUMS/limited market (EMA/CVMP/SWP/66781/2005-Rev.2) [6] was revised in December 2018. The aim of the revision was to take account of the extrapolation criteria considered by CVMP when assessing applications for MRLs as detailed in that Regulation.

***Revision of the guidelines in the context of the VMP Regulation*.**

CVMP considered how the 'limited markets' provision in that Regulation could best be implemented to increase availability of veterinary medicinal products. In November 2019, the CVMP adopted a Concept paper for the revision of scientific guidelines on limited market for veterinary medicinal products (EMA/CVMP/539861/2019) [9] which was available for public consultation until 31 January 2020. In July 2021, the 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 [10] was adopted by CVMP.

Additionally, the CVMP adopted the following guidelines with the date of coming into effect on 28 January 2022:

- 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 [11],
- Efficacy and target animal safety data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of the Regulation (EU) 2019/6 [12],
- Data requirements for applications for immunological veterinary medicinal products intended for limited markets submitted under Article 23 of Regulation (EU) 2019/6 [13], and
- Draft guideline: Safety and residue data requirements for the establishment of maximum residue limits in minor species [14].

Promotion of the MUMS/limited market scheme

As previously mentioned, the policy provided two types of incentives with respect to products classified by CVMP as indicated for MUMS/limited market: reduced data requirements and financial incentives for applications.

MUMS data requirements were applicable to any product that has been classified by CVMP as indicated for a MUMS/limited market. These data requirements were specified in the relevant CVMP guidelines

and generally reduced the amount of data required for authorisation. The extent of reduction would depend on the nature of the product and the indication and therefore applicants were advised to request scientific advice on their individual data package to confirm the precise requirements for their specific product application.

Only products indicated for food producing species were considered eligible for fee incentives where no alternative product was authorised. These financial incentives included free scientific advice and fee reductions for applications for establishing MRLs for minor species and fee waivers for applications for extensions of existing MRLs. The policy specified a list of minor species explaining also fee reductions for submission of marketing authorisation applications under the centralised procedure.

In addition, a greater level of advice and assistance was available for MUMS/limited market products in terms of pre-submission meetings for potential centralised applications and for advice in relation to putting a request together for scientific advice or to establish a Maximum Residue Limit (MRL).

VMP Regulation (EU) 2019/6. Implications for limited markets

Regulation 2019/6 (VMP Regulation) entered into force on 28 January 2019 and became applicable in January 2022. Increasing the availability of veterinary medicinal products is one of the aims of the Regulation which introduces now specific provisions for limited markets, including a definition, conditions and the procedure for granting marketing authorisations, and their renewal.

In the preamble of the VMP 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.*'

The VMP Regulation introduces a specific legal basis for veterinary medicinal products intended for limited markets, a summary of which is outlined below.

- **Article 4 (29)** gives the following definition:

  "(29) '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;"

- **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.

  […]

  6. The competent authority or the Commission, as applicable, may at any time grant a marketing authorisation valid for an unlimited period of time in respect of a veterinary medicinal product authorised for a limited market, provided that the holder of the marketing authorisation for a limited market submits the missing data on safety or efficacy referred to in Article 23(1)."

The VMP Regulation allows for reduced data requirements for the authorisation of a product intended for limited markets on safety and efficacy. The marketing authorisations granted in accordance with Article 23 are valid for a period of five years (and can be renewed). It also allows – once the missing data on safety or efficacy have been provided – to grant a marketing authorisation valid for an unlimited period of time for the same product.

The VMP Regulation introduced some significant changes in comparison to the previously in place: EMA policy and CVMP guidelines, e.g.:

- The applicant is not required to provide all the comprehensive safety or efficacy documentation required in accordance with Annex II of that Regulation;
- Products intended for salmon are considered limited market (as they are classified as minor species) while under the current EMA policy products intended for salmon do not benefit from MUMS classification;
- Marketing authorisations for limited markets are granted for a limited period of time (5 years), which can be renewed;
- No reduction of data requirements on quality is foreseen;
- A statement must be included in the SPC indicating that the marketing authorisation was granted on the basis of a reduced data package;

Discussion

Considering that MUMs/limited market policy was due to expire on 28 January 2022 and the timeframe between obtaining a classification and submission of a marketing authorisation application, it is understandable that the twelfth year of operation showed a significant reduction in MUMS/limited market classification requests.

Nevertheless, continued interest for developing products indicated for limited markets could be observed through the large number of queries received from potential applicants, although understandably less so, submission of new classification requests (Table 1 and Figure 1).

As stated above, the total number of requests for classification significantly decreased in 2021 as the applicants focused on those products or indications for which an initial marketing authorisation application, variation or extension was planned to be submitted and validated before 28 January 2022 while the policy was still valid.

All requests submitted to CVMP in 2021 received a positive outcome, suggesting that applicants understood the upcoming changes and were able to follow the guidance drafted in 2021.

In terms of the financial impact of the policy, the number of requests (re)classified as MUMS/limited market and recommended as eligible for financial incentives (See Table 1 above) observed in 2021 (5 classifications and 1 reclassification) remained the same in comparison to 2020. This was in line with the principle to restrict eligibility for such incentives to products indicated for food producing animals agreed in 2013 and implemented in the revised policy adopted in 2014.

In terms of estimating the total financial impact of the scheme, it is important to note that decisions on eligibility for fee reductions apply only to products submitted through the centralised procedure. Considerations on a possibility for fee reductions for marketing authorisations going through the decentralised/mutual recognition procedure is a matter for the Member States concerned.

Figure 2: Number of centrally authorised products with MUMS/limited market classification 2009-2021*

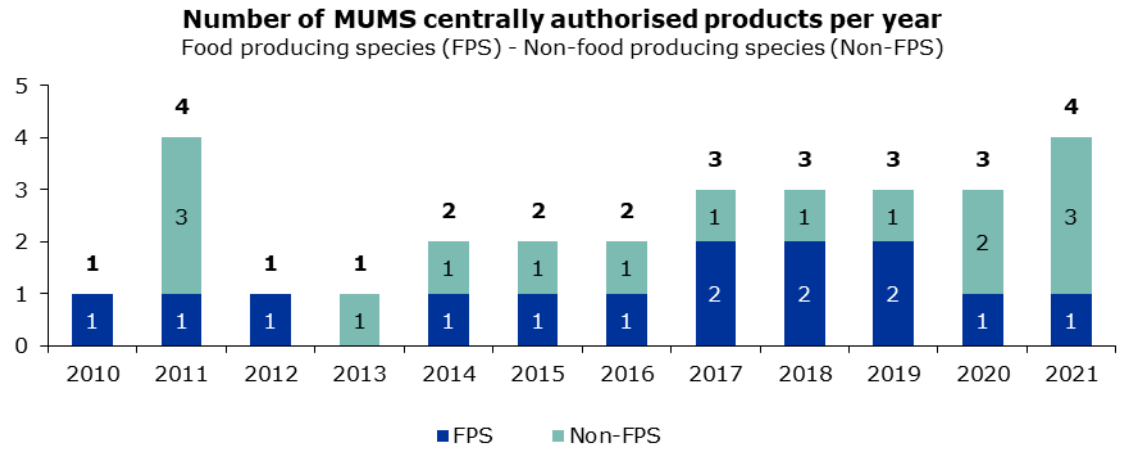


Figure 2 shows the number of veterinary medicinal products with MUMS/limited market classification authorised centrally over the period 2009-2021. It was encouraging to note that there has been a steady stream of products being centrally authorised year on year for MUMS/limited market products (total n=29) in both food-producing (n=14) and non-food producing species (n=15).

Conclusions

The MUMS/limited market scheme remained successful in incentivising the submission of requests for classification or reclassification of products as indicated for MUMS/limited market. These (re)classifications have resulted in newly authorised MUMS/limited market products (or new indications) becoming available for use on the EU market.

A number of requests for products classified in the early years have now been authorised and filled some of the gaps in animal health, meeting the objective of increasing availability of veterinary medicinal products for use on the EU market.

The implementation of the Regulation (EU) 2019/6 in January 2022 has brought the necessity for applicants to re-consider the eligibility criteria for products intended for limited markets. The Agency anticipates that the new legal framework will continue to foster the availability of veterinary medicinal products, and that the companies, utilising advice and assistance from the Agency as well as the newly developed scientific guidance, will continue to bring products intended for limited markets to the EU market.

Annex 1 - References

[1] Revised policy for classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited market, Agency Policy no 75, adopted by Management Board and published on the Agency website (EMA/308411/2014). Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2014/09/WC500172928.pdf

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[8] Guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMA/CVMP/IWP/123243/2006). Available at: https://www.ema.europa.eu/en/data-requirements-immunological-veterinary-medicinal-products-intended-minor-use-minor-species

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[11] 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. Available at: https://www.ema.europa.eu/en/safety-residue-data-requirements-applications-non-immunological-veterinary-medicinal-products

[12] Efficacy and target animal safety data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of the Regulation (EU) 2019/6. Available at: https://www.ema.europa.eu/en/efficacy-target-animal-safety-data-requirements-applications-non-immunological-veterinary-medicinal

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