16 April 2018
EMA/CVMP/370663/2009–Rev.4
Veterinary Medicines

Q&A - EMA guidance for companies requesting classification for products/indication as Minor Use Minor Species (MUMS)/limited market

Introduction

This guidance document addresses a number of questions that applicants requesting classification of products/indications for minor use or minor species (MUMS)/ limited market may have.

The Committee for Medicinal Products for Veterinary Use (CVMP) classifies applications in line with European Medicines Agency 'Revised policy for classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited markets (EMA/327514/2013 Adopted) and the EMA provides procedural and financial assistance accordingly. This policy has been endorsed by the EMA Management Board and is intended to stimulate MUMS/limited market applications which otherwise would not be developed.

This guidance document for companies requesting classification for MUMS/limited market provides an overview of the procedure to obtain classification and gives guidance to applicants in preparing their request. It also sets out what assistance of a procedural and/or financial nature may be provided. Furthermore, applicants will be guided through the different steps of the procedure and receive relevant information for the preparation of a request for classification or for reclassification after the original 5 year period of classification had come to an end for MUMS/limited market.

The EMA constantly reviews the criteria for eligibility for access to incentives and amends the policy as appropriate. Since September 2013 only products indicated for food producing species have been eligible for fee incentives in line with the latest revision of the policy at that time.

It should be highlighted that this document has been produced for guidance only and should be read in conjunction with applicable policies and legislation.

References and useful links

- Regulation (EC) 726/2004 of the European Parliament and Council of 31 March 2004.
- European Parliament and Council Directive 2001/82/EC of November 2001, as amended.
- Revised policy for classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited market (EMA/308411/2014).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

- Position Paper regarding availability of products for Minor Uses and Minor Species (MUMS) (EMA/CVMP/477/03-Final).
- Guidance on the classification of veterinary medicinal products indicated for minor use minor species (MUMS) / limited market (EMA/CVMP/388694/2014).
- "Scientific Advice to be given by the CVMP for Veterinary Medicinal Products" (SOP/V/4016).
- Commission Regulation (EC) No 2049/2005 laying down rules regarding the payment of fees to, and the receipt of administrative assistance, from the European Medicines Agency by micro, small and medium-sized enterprises (link).
- Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the EMA (link)
- Explanatory note on fees payable to the European Medicines Agency (link).
- Request to the CVMP to (re)classify a veterinary medicinal product/indication as MUMS/ limited market (form).

CVMP MUMS data requirement guidelines

- Guideline on quality data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMA/CVMP/QWP/128710/2004).
- Guideline on safety and residue data requirements for pharmaceutical veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMA/CVMP/SWP/66781/2005).
- Guideline on efficacy and target animal safety data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMA/CVMP/EWP/117899/2004).
- Guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species (MUMS)/limited market (EMA/CVMP/IWP/123243/2006).

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1. What is the definition of a MUMS/limited market product/indication?

Minor species

There is no legislative definition in the EU for major or minor species. However, major species were defined by the CVMP according to animal population data and total consumption figures, using global numbers across the European Union for the purpose of CVMP guidelines in its position paper regarding availability of products for Minor Uses and Minor Species (MUMS) (EMEA/CVMP/477/03-Final). All other animal species, which are not considered major, are as a consequence, by default, classed as minor species.

Major food-producing species:

- cattle (dairy and meat animals);
- sheep (meat animals);
- pigs;
- chickens (including laying hens);
- salmon[1].

Major companion animal species:

- cats;
- dogs.

The CVMP will apply these definitions when deciding on eligibility for MUMS/limited market classification for veterinary medicinal products.

Applicants may apply for classification in relation to products for minor species either when seeking authorisation of a new product indicated only for one or more minor species or when extending an existing authorisation to a new, minor species.

Minor use

Minor use in a major species is generally considered as the use of veterinary medicinal products for the treatment of diseases that occur infrequently or occur in limited geographical areas and thus are indicated for a smaller market sector. The minor use of a product/indication will be considered on a case-by-case basis taking into account justification put forward by an applicant to support the minor use of a product/indication in line with the procedure outlined.

The CVMP will use the following factors in reaching a decision if an indication can be considered minor use:

- Low prevalence/incidence of the condition or disease within the EU:
  - low prevalence may result from the natural epidemiology of the disease or may be the result of control measures at national, regional or community level;
  - treatments with low prevalence/incidence would be expected to have a low return on investment (ROI) but this is considered as an indirect factor;
- Limited geographical spread of the disease within the EU in one or a few areas.

[1] Salmon should be considered a major species, however other species of the *Salmonidae* family such as rainbow trout should be considered minor species.

Limited market

Consideration if the market for a product can be classified as limited is taken as a next step following the consideration if it the product is indicated for MUMS (please see Figure 1, page 9).

The term limited market includes all situations in which the market for a veterinary medicinal product is limited in terms of size and therefore includes products for minor indications including those with a limited geographical distribution (e.g. leishmaniosis in dogs), and the great majority of those indicated for minor species (e.g. rabbit haemorrhagic disease in rabbits).

In rare cases, the CVMP may decide that although a product is indicated for a minor species, the market for the product is not limited (e.g. anthelmintics for horses). The CVMP will gain experience based on applications made with a view to developing more objective criteria for classifying a market as limited.

Included within the definition of 'limited market' are some products for which the market is limited due to the fact that the diseases concerned are subject to community control although the disease itself may not be considered 'minor' in nature (e.g. Classical Swine Fever, Foot-and-Mouth-Disease, Bluetongue, avian influenza). For these diseases, the limited nature of the market is the result of a combination of legal, market and technical factors. Appropriate measures to assist applicants to authorise products for these diseases are developed on a case-by-case basis (e.g. data requirements, exceptional authorisation, fee incentives, multistrain dossier approach) and they are not considered to fall within the scope of this paper unless they meet the definition of MUMS, above.

2. How can a company request classification? Can I have a pre-submission meeting?

A request for classification in order to avail of the incentives offered should be addressed to the Veterinary Medicines Department at the European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5EU, UK or by email to VetMUMSapplications@ema.europa.eu.

The request should be sent to EMA 20 days in advance of the CVMP meeting (dates of the monthly CVMP meeting are published on the EMA website) in order to be considered at the next CVMP meeting.

The request (one electronic copy) should be presented as follows:

1. Cover letter;
2. The classification request form (link) as published on EMA website as Word file duly completed; the template may not be exhaustive in all cases and additional supportive evidence may be provided.

   The template includes background information on the applicant and product profile of the veterinary medicinal product (pharmaceutical, biological or immunological).

Pre-submission advice

The EMA can advise in advance of any request should applicants have any questions as to what information should be provided.

The companies can also request pre-submission meetings. However, the experience has shown that usually all questions can be addressed by contacting: VetMUMSapplications@ema.europa.eu.

3. What is the timetable for classification?

Requests for classification that are received 20 days in advance of the CVMP meeting will be considered at the nearest upcoming CVMP meeting.

For straightforward requests the CVMP will make the decision and classify the product/indication as MUMS/limited market and the applicant will be informed immediately following that CVMP meeting by the EMA secretariat.

In some more complex cases, there may be a need to appoint a CVMP member to review in more detail the request and provide a recommendation to the CVMP. This will normally be done within one month and the applicant will then be informed of the outcome. It is also envisaged that additional information may need to be requested in some cases and the timetable will then depend on the timing of the response of the applicant with the requested information.

4. Is there a fee for classification?

No, there is no fee for classification, nor any fee for any related advice from the EMA in advance.

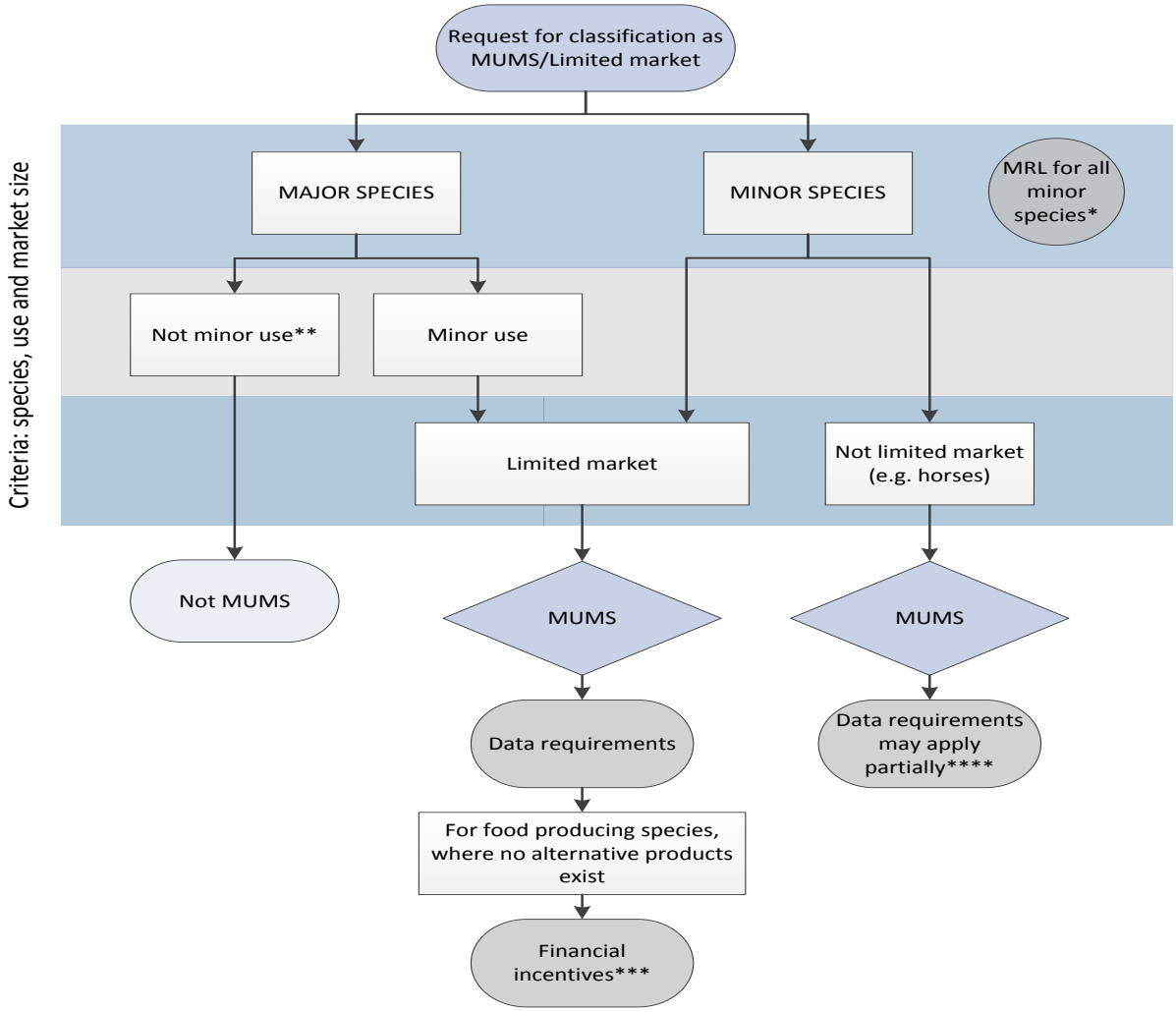
5. How will my request be evaluated?

The requests received will be evaluated by CVMP in accordance with the definitions of MUMS/limited market agreed. Requests will be evaluated based on the information provided by the applicant in the completed template.

In some more complex cases, there may be a need to appoint a CVMP member to review in more detail the request and provide a recommendation to the CVMP. It is also envisaged that additional information may need to be requested in some cases.

The evaluation will be based on the criteria set out in the template to be completed including target species indicated (major or minor), prevalence of the condition in the EU including geographical distribution (minor use), potential market size and return on investment (limited market), use in food producing animals (financial incentives) and current or alternative therapies available.

Figure 1.



* MRL application: MUMS data requirement apply for all minor species (MUMS and not MUMS)

** For diseases which do not inherently have a low incidence or prevalence but the market in the EU is limited and in such cases the product/indication may be indicated for MUMS/limited market – see (EMA/CVMP/388694/2014) Definition of limited market

*** Products for horses are generally not eligible for MUMS fee incentives

**** Applicants are advised to seek scientific advice on the extent to which MUMS data requirements would apply. No financial incentives will apply.

Examples of centrally authorised products/indications classified as MUMS/limited market:

Varroosis in honey bees (minor species);

Colibacillosis in turkeys (minor species);

Myxomatosis and rabbit haemorrhagic disease in rabbits (minor species);

Mast cell tumours in dogs (minor use);

Fibrosarcoma in cats (minor use);

Aspergillosis and candidiasis in birds (minor species/minor use);

Leishmaniosis in dogs (minor use).

6. Can an applicant appeal the decision?

Yes, a re-examination procedure is available for an applicant where classification of a product/indication is rejected by CVMP. Applicants may ask for re-examination of the decision on classification by written request to CVMP within 60 days of receipt of the notification letter. The applicant has to provide detailed grounds for re-examination. He may also provide additional data to substantiate any grounds on which re- examination is made. The timetable for the CVMP consideration of the re-examination will be similar to an initial request. The outcome of the re-examination will then be notified to the applicant.

7. What benefits are there in classification?

There is no obligation to request classification as a MUMS/limited market product unless an applicant wishes to avail of the incentives provided under these initiatives, which are valid for up to five years once classification is confirmed. Any benefits outlined here can only be granted within the time period when the product/indication has a valid MUMS classification. The incentives provided include a greater level of advice and assistance for these products/indications in terms of pre-submission meetings for potential centralised applications and advice in relation to putting an application together for any type of application, including where scientific advice or MRL applications are being considered. Other benefits include:

A. MUMS data requirements

The confirmation of data requirements is an important measure to assist applicants. Products/indications classified by CVMP as indicated for MUMS/limited market should refer to the CVMP guidelines on data requirements for MUMS. Applicants may also request scientific advice on their individual data package.

B. Financial incentives

Financial incentives are limited to MUMS products /indication intended food producing animals since September 2013.

Current information on actual fees, fee reductions or waivers can be found in Explanatory note on fees payable to the European Medicines Agency (EMA/458574/2013).

Pursuant to Article 70.2 of Regulation (EC) No 726/2004 of 31 March 2004, SMEs are eligible for fee reductions, fee deferrals and conditional fee exemptions in accordance with Regulation (EC) No 2049/2005 of 15 December 2005. If a company is eligible for SME designation it is advisable to apply for SME registration in addition to a MUMS classification for a specific product/indication and thus gain full advantage on all available incentives. It should be noted that fee incentives can only be considered once the applicant has been assigned SME status by the EMA. Information for additional financial and other incentives to SME companies can be found on SME website (link).

B.1 Free scientific advice

There will be no fee for scientific advice for products/indications indicated for MUMS/limited market and eligible for financial incentives.

The standard application procedure will apply (see EMA guidance for companies requesting scientific advice - link). Scientific advice may also specifically be requested for an application relating to the published guidelines on dossier requirements in the areas of quality/safety/efficacy and immunologicals. These requests will enable an applicant to put together an outline of their dossier and to receive assurance that the proposed dossier will contain the necessary information for authorisation in compliance with the possibilities for the reduction of data in the different sections of the dossier. The fee for assessing compliance of a proposed data package with the relevant published CVMP guidelines on data requirements for veterinary medicinal products intended for MUMS/limited market will be waived for eligible products/indications.

B.2 MRL applications (including extrapolation)

In relation to a substance intended to be included in a product classified by CVMP as indicated for MUMS/limited market, the applicant can, obtain:

- **Fee exemption in the event of failure of validation**

Exemptions are already available for SMEs intended to reduce the risk to applicants in applying for MRLs.

- **Fee reduction for the MRL applications**

A fee reduction of 50% is applicable for MRL applications for a new active substance intended exclusively for a product classified as MUMS/limited market where MUMS status has been confirmed by CVMP and for applications for the extension of an existing MRL to a minor species where the need to assess new data exists.

Requests for the extension of MRLs without provision of new data, i.e. the establishment of existing MRLs in an additional, normally minor, species based on existing data and provided that the criteria as described in the CVMP note for guidance on the risk analysis approach for residues of veterinary medicinal products in food of animal origin (EMEA/CVMP/187/00-FINAL) have been fulfilled, will be processed by the EMA/CVMP free of charge.

B.3 Centralised marketing authorisation application

If eligibility for the centralised marketing authorisation procedure is confirmed by CVMP for an application that concerns an indication the CVMP has previously classified as MUMS/limited market, the applicant can apply to obtain:

- **Fee exemption in the event of failure of validation**

Fee exemptions will be given in the event of failure of validation of a dossier for a marketing authorisation.

- **Fee reduction for authorisation and for maintenance**

For MUMS/limited market applications 50% reduction for authorisation and 75% reduction for maintenance applies. This measure will also apply to applications for extensions of existing centralised products to add a food producing minor species but the maintenance fees will remain as for the initially authorised product.

A centralised application that concerns more than one target species at the time of submission, only one of which is MUMS, will not attract a reduced fee as the current fee structure is set up so that additional target species do not attract an additional fee. The fee charged will therefore reflect that the product is not exclusively indicated for MUMS/limited market.

8. How long is the classification valid for?

The classification is valid for five years from the decision of CVMP.

It is necessary to set a reasonable period of validity to provide applicants with the predictability they require to invest in bringing a new product to market. Conversely, it is necessary periodically to review the classification of indications to take into account changes in the market for, or epidemiology, of the condition concerned.

The Agency aims to contact applicants approximately 6 months prior to the expiry of the 5 year classification time period by sending a reminder letter which outlines options available to each applicant.

9. Will the classification be published?

Yes, the classification will be published in order to be transparent in line with the EMA policy and to allow potential applicants to view previous decisions on classifications. The outcome of the request for consideration for MUMS/limited market classification will be published in the press release of the relevant CVMP meeting in general terms stating the indication and/or therapeutic area (since 2016 at Level 1 of the ATCVet Code), the target species and whether or not the CVMP considered that the product/indication was indicated for MUMS/limited market. This information will also be published in the EMA annual report as part of a report given to the EMA Management Board of measures provided by the Agency to applicants to assist with authorisation of products for limited markets under Article 79 of Regulation 726/2004.

A table of decisions related to these applications is maintained on the EMA website at:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000499.jsp&mid=WC0b01ac05803ddc15

Details of the applicant, indication and active substance are not published prior to adoption of an opinion on the respective product by CVMP. Following adoption, full details are included in the European Public Assessment Report (EPAR) that is published on the EMA website. This EPAR also includes information on the basis on which the opinion was reached including the extent to which MUMS data requirements were applied as part of the assessment procedure.

10. Will more than one classification be given for the same indication in the same target species?

Yes, where an applicant submits a request for classification and the application is deemed to comply with the criteria in place, then the product will be classified, irrespective of the fact that another product for the same indication in the same target species may already be classified.

However, once a product has been authorised by a licensing authority for that indication in the target species within EU, no financial incentives will be granted for any new classifications as a product will already be available in the marketplace for the proposed indication. Products which have already been classified prior to the first authorisation may, however continue to benefit from the financial incentives in place until the original 5 year period of classification comes to an end.

11. Do I have to confirm the route of authorisation - centralised / decentralised / national?

An applicant may request classification for any product/indication irrespective of the intended route of authorisation. MUMS data requirements apply to any product/indication classified by CVMP as MUMS/limited market. Likewise, fee waivers apply for eligible applications for scientific advice from CVMP whether the application to which the advice refers is intended to be submitted through the centralised or national procedures. This includes scientific advice on compliance of a proposed data package with the respective CVMP guidelines on MUMS data requirements. In view of the different ways in which MUMS applications are handled in different Member States, applicants are advised to consult with the respective national authorities with respect to any application relating to a MUMS product intended to be submitted through a national procedure.

Specific incentives that relate to the centralised procedure will be dependent on the veterinary medicinal product having shown eligibility for the centralised procedure. Requests for eligibility to the centralised procedure should be sent in the usual way (see pre-submission guidance documents on EMA website link).

12. Does MUMS status in other regions e.g. FDA / other regulatory authorities influence my application?

The MUMS policy (EMEA/CVMP/477/03-Final) defines the criteria for classification of products/indications as MUMS/limited market in the EU/EEA. MUMS status awarded in other regions is not a criterion that will be taken into account directly as both the classification of major and minor species and the prevalence and incidence of a disease may differ between regions. Information on the MUMS status of a product/indication in other regions and the rationale on which this status was granted should therefore be provided to CVMP as supporting information only.

13. How are horses addressed under this policy?

Horses are considered a minor species and products/indications for horses are therefore eligible for MUMS data requirements. As with all MUMS products, the actual level of data requirements will depend on the particular product and applicants will it is therefore recommended to seek scientific advice on the specific data requirements that would apply.

Although horses are formally a food producing species, most products indicated for horses in the EU are administered to horses at a time when their ultimate fate with respect to the food chain is unknown. Only a minority of products are administered to horses that are clearly destined for the food chain at the time of treatment. Horses will therefore not be considered as food producing animals within the scope of the revised MUMS policy and products for horses will therefore not generally be eligible for fee incentives.

In exceptional cases, applicants may request fee incentives on the basis that they intend to make (an) MRL application(s) so that the product concerned can be used in horses that are intended for the food chain. This specific exemption from the general approach is intended to support the objective of increasing the availability of products that can be used in horses which ultimately enter the food chain, whether their ultimate fate is known at the time of treatment or not.

14. When should I apply for scientific advice with respect to a MUMS product/indication?

Applicants should in the first instance apply for classification of their product under the MUMS/limited market policy in order to avail of the incentives offered related to scientific advice. These incentives may be taken up at any time in the five years after classification. Requests for scientific advice will be free for products eligible for financial incentives and applicants are requested to complete the template for requests for scientific advice as published on the EMA website and return this to the EMA at least one month in advance of any request being submitted – please see Guidance for companies requesting scientific advice (EMEA/CVMP/172329/2004-Rev. 4).

15. Where can I get advice on applicable MUMS data requirements for MUMS/limited market?

CVMP has adopted guidelines on MUMS data requirements which may be applicable to products being developed for MUMS/limited market. These guidelines are published on the EMA website "Scientific guidelines" and applicants may request advice on the application of these guidelines to the specific product under development. These requests should be submitted as scientific advice requests and will be free of charge for products for food producing animals classified as MUMS/limited market by CVMP and eligible for the financial incentives.

16. What is the procedure for establishment/extension of an MRL for MUMS/limited market?

In order to establish a new MRL or to extend an existing MRL for a substance intended to be used in a MUMS/limited market product the standard application procedure will apply. In order to qualify for a fee reduction the applicant should submit a request to the CVMP, requesting classification of the product/indication for which the substance in intended as indicated for a MUMS/limited market (see Question 1). Relevant applications relating to MRLs will automatically be eligible for MUMS fee incentives as MRLs are only required in the case of products indicated for food producing animals. If the classification is granted, then in the application the applicant should include that the substance has been classified as intended for MUMS/limited market, and a fee reduction of 50 % will then be applied for the new MRL procedure. Requests for the extension of MRLs without provision of new data, i.e. the establishment of existing MRLs in an additional, normally minor species based on existing data should comply with the criteria as described in the CVMP note for guidance on the risk analysis approach for residues of veterinary medicinal products in food of animal origin (EMEA/CVMP/187/00-FINAL).

For full details of the procedure please read the regulatory guidance on the EMA website for MRL applications (link).

17. How to request a fee reduction for a centralised submission or extension?

Requests for a fee reduction for a centralised submission of a product classified as MUMS/limited market should be submitted in the usual way along with the letter of intent to submit a marketing authorisation application to CVMP. The European Medicines Agency recommends providing the notification of intent **at the latest 7 months** before submission of the marketing authorisation application (MAA) (see pre-submission guidance documents on EMA website link).

18. Can the MUMS status be renewed after the original 5-year period expires?

Yes, further to the Question 8, the Agency aims to contact applicants by sending them a reminder letter prior to expiry of the classification. The letter is to prompt applicants to review the ongoing need for the classification and whether in the past 5 years there were any changes with regards to the data in their original application.

The applicants will need to fill in the (re)classification request template (published on the EMA website) and submit it to VetMUMSapplications@ema.europa.eu.

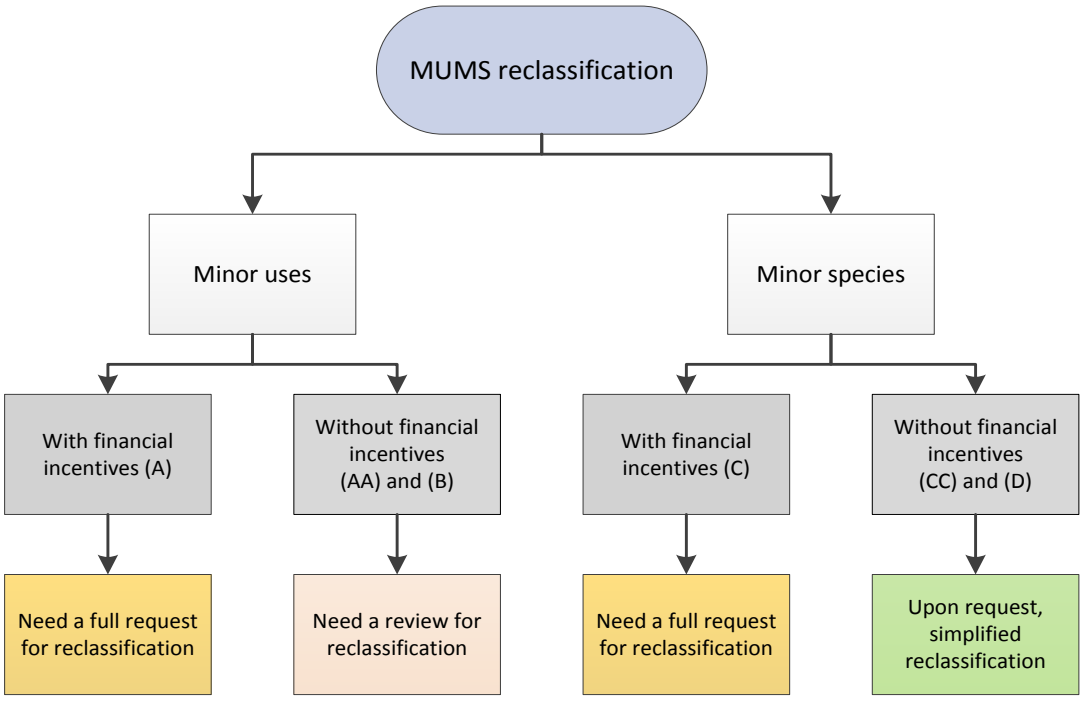
Please note that the reclassification request template asks to summarise any changes over 5 years in the epidemiological/disease/disorder status relevant to the product indication and whether or not alternative products have been authorised for the condition concerned since the date of last classification. Additionally, the applicants will be asked to provide a report on sales volume data/number of treated animals as reported on periodic safety update reports (PSURs) for authorised products or a report on a current state of development of the product (i.e. what studies have been done).

The requests for reclassification, especially for those products/indications with financial incentives, should be submitted well in advance of the expiry. When planning to submit a reclassification request, please note that any applications received at least 20 days prior to the CVMP meeting will be considered at that meeting. Those submitted later will be deferred to the next consecutive meeting.

Please note that under the current policy as published, financial incentives are currently restricted to food producing species only.

The exception to the above procedure, are classifications without financial incentives for minor species. For simplicity, these will only require confirmation by the applicant whether there is still an ongoing need for this classification. Upon receipt of such confirmation EMA will put forward a request to CVMP for reclassification for the further 5 years.

Figure 2.



19. If my product has been authorised within the original 5-year period do I need to submit a reclassification request?

With that expiration of MUMS/limited market classification any financial and data requirement incentives cease under the Agency policy. Therefore, it is advisable that the applicants review the ongoing need for reclassification and if still considered necessary, submit their request to EMA well in advance of the of the expiry date.

For authorised products intended for food producing species applying for reclassification can be beneficial as they may still be entitled to financial incentives.

For authorised products intended for non-food producing species reclassification can be beneficial if they plan submission of post-authorisation applications where there may be a benefit from the reduced data requirements.

Moreover, it is worth noting that as at the time of submission of a marketing authorisation the MUMS classification was valid, and a product in consequence has been authorised as MUMS product (or with a MUMS indication), it will be referred to as such in the future (i.e. in EPAR), even if the MUMS classification expires.

20. Is the MUMS classification transferable?

MUMS/limited market classification is granted to the product/indication and therefore transferable together with the product.

Provided that the sponsor/applicant (owner) is the only aspect/characteristic of the product that changes in result of the transfer, the MUMS/limited market classification for the product is transferable.

In case any other aspect/characteristic has changed in the meantime, we advise the current owner to contact EMA, clearly identifying any such change, for EMA to advise the current owner on whether the current classification still applies or not to this product and on any other required actions.

To formally acknowledge the transfer, EMA need a letter from the original owner officially informing of the transfer of the ownership of the product and the MUMS/limited market classification from the original owner to the current one. This letter should state MUMS outcome letter document reference number.