Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

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BEST PRACTICE GUIDE

for

The classification of unforeseen variations

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[1] Amending Regulation (EU) No. 712/2012 to the Variation Regulation applies from 2 November 2012

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1. INTRODUCTION

Article 3 paragraph 1 of Commission Regulation (EC) No 1234/2008 (variation regulation) refers to Annex II where a classification of minor variations, type IA, and major variations, type II, is laid down. The classification of extensions of a marketing authorisation is laid down in a list in Annex I. Article 4 of the variation regulation confers on the Commission the obligation to establish guidelines on the details of the various categories of variations (classification guideline). These guidelines shall be regularly updated, taking into account the recommendations of the CMDv and CMDh or, in the case of centralised marketing authorisations, the EMA.

Article 5 of the variation regulation, and the subsequent amending Regulation (EU) 712/2012, provides the basis for a marketing authorisation holder (MAH) to request the Reference Member State (RMS), EMA (in case of centralised marketing authorisations) or a national competent authority of a Member State (NCA) (in case of purely national marketing authorisations) to deliver a recommendation on the classification of a variation whose classification is not provided for in the regulation (unforeseen variation) before submission of the variation. This recommendation shall be consistent with the Commission guidelines and be delivered to the MAH, EMA, CMDv and CMDh within 45 days following the receipt of the request.

Article 5 of the variation regulation also provides the basis for a NCA to request the CMDv or CMDh to deliver a recommendation on classification of an unforeseen variation before examination of the variation. This recommendation shall be consistent with the Commission guidelines and be delivered to the MAH, EMA and all NCAs within 45 days following the receipt of the request.
Cooperation between the two coordination groups and the EMA is envisaged by the legislation. The recommendations will be published once adopted.

It should be noted that the recommendation of the CMDv is not a pre-assessment of the future variation application but a recommendation of the classification of a variation. The recommendation relates to the situation described in the request.

2. SCOPE

This guidance covers medicinal products for veterinary use that have been authorised through the mutual recognition, decentralised or purely national procedures. The request shall apply only to variations whose classification is not provided for in the above mentioned annexes (unforeseen variations). The CMDv cannot “reclassify” a variation already listed in the annexes/guidelines.

3. SUBMISSION & VALIDATION OF REQUEST FROM A MAH

A request for a recommendation for a classification from a MAH shall be submitted to the relevant authority prior to submission of the variation.

The application form for Article 5 requests, published on the CMDv website (http://www.hma.eu/163.html), should be used. It is important that the request includes a detailed description of the product and a detailed description of the proposed variation of the terms of the authorisation, as there is no time within the prescribed timetable to request

additional information. The request should include information detailing whether a similar variation previously has been submitted to a NCA and if so how it was classified and in accordance with which guidance. The request should, in addition, include a justification of why the variation is considered to be unclassified according to the variation regulation; and a proposal for a classification for this variation.

It is the responsibility of the relevant authority to validate the request with respect to the classification guideline.

Invalid request :

- If the relevant authority considers the variation to fall under the scope of a foreseen variation.
- If a recommendation has already been issued.
- If the variation should clearly be classified as type IB by default according to the classification guideline, the authority will deem the request invalid and inform the MAH thereof.

Valid request : if the relevant authority considers the variation to be unclassified, it is recommended that the request is forwarded to the coordination group for discussion in order to avoid any discrepancies in recommendations. This should be done at the latest within 25 days following receipt of the request in order to have no less than 45 days left for the CMDv phase. The timetables for Article 5 recommendations are published on the CMDv website. See also the flow chart in annex 1 “Flow chart for recommendations on unforeseen variations - request to CMDv from a MAH”.

4. SUBMISSION OF REQUEST TO CMDv FROM NCA

A request for a recommendation of a classification from a NCA shall be submitted to the CMDv secretariat electronically (CMDv@ema.europa.eu) prior to examination of a variation or following a valid request from a MAH. The NCA request should comply with the submission details described under section 3 above. The CMDv secretariat will forward the request for a recommendation to the All Veterinary ART5-VARIATIONS mailbox.

The CMDv is obliged to issue a recommendation within 45 days of the receipt of the request. In order for the CMDv to have the opportunity to discuss the request at one of their monthly meetings, specific submission dates should be adhered to. These will be published on the CMDv website.

5. HANDLING OF REQUEST AND COOPERATION WITH CMDh AND EMA

5.1. Request made to CMDv

The NCA that received the request from a MAH or that triggered the article 5 procedure will be the Rapporteur.

The CMDv secretariat shall without delay distribute the request to all the CMDv members, the secretariat of CMDh and the contact point at EMA for information.

It is recognised that in particular Quality related variations could have an impact on other groups and it is essential that appropriate consultation takes place before a recommendation is adopted by CMDv.

5.2. Request made to CMDh

Where the CMDv secretariat receives notification of a request submitted to CMDh or EMA, they will circulate details of that request to CMDv members. If the request involves a variation that may impact on the veterinary side then a CMDv rapporteur may be appointed. CMDv members will then provide comments to the rapporteur, who in turn would coordinate and forward a CMDv response to the CMDh secretariat. In all other cases comments would be sent by individual members directly to the CMDh secretariat.

6. THE RAPPORTEUR

The rapporteur shall propose a recommendation for a classification with an appropriate justification, on consideration of the facts presented to it in the request from the MAH or the NCA while ensuring consistency with the Commission guidelines on categories of variations.

The proposal for a recommendation for a classification should be sent to the All Veterinary ART5-VARIATIONS mailbox according to the timetable for the procedure. The secretariat will forward the proposal for classification to CMDh members and the EMA contact point.

7. MEMBER STATES COMMENTS

All CMDv members, CMDh members and the EMA may send comments on the rapporteur's proposal for a recommendation for a classification. The comments must be sent according to the timetable for the procedure to the All Veterinary ART5-VARIATIONS mailbox. If a CMDv or CMDh member or EMA has a divergent view from the rapporteur this should be properly justified.

8. DISCUSSION AT CMDv MEETING

The EMA, members of CMDh and European Commission shall be invited to the discussion at CMDv. National experts may attend in the same manner as for referral procedures. No participation from the MAH is anticipated.

Members of CMDv should have a mandate to express the view of the Member State[2]. In case of divergent opinions among members of the CMDv the voting procedure in the Rules of Procedure shall apply.

It should be noted that CMDv is not empowered to issue a decision but to deliver a recommendation according to article 5 of the variation regulation. However it is expected that the MAH will accept and follow the recommendation of the CMDv.

9. THE RECOMMENDATION

Groups should use their best endeavours to reach a harmonised position. In cases where there is a divergent opinion between CMDv / CMDh / EMA the recommendation shall include both arguments in order that the Commission could take an informed decision based on the points of view of both CMDs and EMA, when drawing up or updating guidelines referred to in Article 4(1) (a) of the regulation.

[2] It is expected that prior discussion within the respective agency would have already taken place.

After the CMDv discussion, the Rapporteur updates the recommendation to reflect the outcome of the discussion and sends the final agreed CMDv recommendation including the information for publication to the designated mailbox.

The recommendation should include the conditions applicable for the recommended classification of the variation but not the required documentation.
The CMDv secretariat will distribute the CMDv recommendation to the MAH or NCA who made the request, CMDh, the EMA and the European Commission. This should be done on Day 45 of the timetable of the procedure to ensure the timeframe as stated in Article 5 of the variation regulation can be met.

There is no possibility to appeal a recommendation issued by the CMDv.

10. PUBLICATION OF RECOMMENDATIONS

Recommendations from CMDv shall be published on the CMDv website and be mentioned in the monthly CMDv report for release, to ensure ease of accessibility. Information of commercially confidential nature has to be deleted.

Recommendations from CMDh with impact on the Veterinary sector shall also be published as a link on the CMDv website.

11. CLASSIFICATION OF VARIATIONS ANNEX II REGULATION 1234/2008, as amended

It is the responsibility of the Commission to initiate regular updates of the guideline referred to in Article 4 point (a) and Annex II of the variation regulation taking into account the recommendations adopted by the CMDv, CMDh and EMA.

ANNEX 1

FLOW CHART FOR RECOMMENDATIONS ON UNFORESEEN VARIATIONS - REQUEST TO CMDv FROM A MAH

Day -25	MAH sends a request to NCA electronically.
Between Day -25 and Day 0	NCA (= the Rapporteur) performs validation of request and, if valid, forwards it to the CMDv. If not valid, the request will be refused and the applicant informed accordingly. The Rapporteur circulates the valid request to the CMDv secretariat (cmdv@ema.europa.eu) The CMDv secretariat will forward the request for a recommendation to the All Veterinary ART5-VARIATIONS mailbox.
Day 0	CMDv secretariat circulates the request with the adequate timetable to: • the Rapporteur • all CMDv members • the CMDh secretariat • the EMA contact point
Day 25	The rapporteur makes a proposal for the classification of the variation. The rapporteur circulates this proposal to the All Veterinary ART5-VARIATIONS mailbox.
Day 32	The rapporteur receives the comments from • all the CMDv members • all the CMDh members • the EMA contact point
Day 38/39	Discussion at the plenary meeting of the CMDv. Final position on the recommendation.
Day 42/43	The Rapporteur circulates the updated final recommendation via the designated mailbox. In cases where there remains a divergent opinion between CMDv / CMDh / EMA the CMDv secretariat sends the recommendation including the arguments to the European Commission for information.
Day 45	• The NCA (Rapporteur) communicates the outcome to the MAH. • The recommendation is published on the CMDv website.