

CMDv/BPG/015

BEST PRACTICE GUIDE
for
The classification of unforeseen variations

Edition number: 01

Edition date: 11 January 2011

Implementation date: 01 January 2009

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1. INTRODUCTION

Article 3 paragraph 1 of Commission Regulation (EC) No 1234/2008 of the variations regulation refers to Annex II where a classification of minor variations, type 1A, 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 places an obligation on the Commission to establish guidelines on the details of the various categories of variations. 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 variations regulation provides the basis for a marketing authorisation holder (MAH) or a competent authority of a Member State (NCA) to request CMDv, CMDh or EMA to deliver a recommendation on the classification of a variation whose classification is not provided for in the regulation (unforeseen variation). This recommendation shall be consistent with the Commission guidelines and be delivered 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 shall be published once delivered.

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

2. SCOPE

This guidance covers mutual recognition and decentralised medicinal products for veterinary use. 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 OF REQUEST

The request for a recommendation for a classification from the MAH or the NCA shall be submitted to the CMDv secretariat electronically at CMDv@ema.europa.eu, prior to submission or examination of the variation. It is recommended that the application form for Article 5 requests published on the CMDv website (<http://hma.eu>) is 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. The request should, in addition, include a justification of why the variation is considered unforeseen; and a proposal for a classification for this variation. 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 (see annex 1). These will be published on the CMDv website (<http://www.hma.eu/typo3/backend.php>) .

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4. HANDLING OF REQUEST AND COOPERATION WITH CMDh AND EMA

4.1 Request made to CMDv

One member of CMDv shall be appointed as rapporteur and propose a recommendation for a classification of the variation¹. The CMDv secretariat shall without delay send the request and details of the Rapporteur to all CMDv members. The secretariat will also circulate the timetable for dealing with that request. Should a NCA make the request, it will not be possible for that Member State to act as the rapporteur. The secretariat will send information via the CMDv mailboxes. If the appointed rapporteur can not undertake the evaluation it will be the responsibility of the rapporteur to make alternative arrangements, but they will remain the primary contact for communication.

The CMDv secretariat shall without delay distribute the request to the secretariat of CMDh and the contact point at EMA, which in turn will notify the relevant EMA bodies.

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.

4.2 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.

5. 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.

6. 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.

¹ The secretariat will hold a list of members and these will be allocated in rotation.

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7. 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 State². 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.

8. 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.

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.

9. 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.

10. ANNEX II – CLASSIFICATION OF VARIATIONS

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.

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

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ANNEX 1

FLOW CHART FOR RECOMMENDATIONS ON UNFORESEEN VARIATIONS - REQUEST TO CMDv

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	MAH or NCA send a request to CMDv electronically.
Day 0	CMDv secretariat receives the request by e-mail. CMDv secretariat nominates a rapporteur within the list. CMDv secretariat sends the request with the adequate timetable to the relevant mailboxes for: <ul style="list-style-type: none"> all CMDv members the CMDh secretariat the EMA contact point (CLAG inbox)
Day 25	The rapporteur makes a proposal for the classification of the variation. The rapporteur sends this proposal to the All Veterinary ART5-VARIATIONS mailbox.
	The CMDv secretariat sends this proposal to: <ul style="list-style-type: none"> the CMDh secretariat the EMA contact point
Day 32	The rapporteur is in receipt of the comments made by <ul style="list-style-type: none"> 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 45	The CMDv secretariat sends the recommendation to: <ul style="list-style-type: none"> the MAH or NCA who made the request. all CMDv members the CMDh secretariat the EMA contact point the European Commission.
	The recommendation is published on the CMDv website.

Time line for request received by CMDv

<http://www.hma.eu/typo3/backend.php>

Time line for request received from CMDh

The submission of CMDv comments should follow the CMDh timetable.

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ANNEX 2

RECOMMENDATION OF THE CMDv ON THE CLASSIFICATION OF AN UNFORESEEN VARIATION

**RECOMMENDATION OF THE COORDINATION GROUP FOR MUTUAL
RECOGNITION AND DECENTRALISED PROCEDURES - VETERINARY
(CMDv)
ON THE CLASSIFICATION OF AN UNFORESEEN VARIATION
TO THE TERMS OF THE MARKETING AUTHORISATION**

Name of the medicinal product in the RMS <i>(if applicable)</i>	
INN (or common name) of the active substance(s) <i>(if applicable)</i>	
Pharmaceutical form(s) and strength(s) <i>(if applicable)</i>	
Reference Number for MRP/DCP <i>(if applicable)</i>	

BASIS FOR THE RECOMMENDATION

Pursuant to Article 5 of Commission Regulation (EC) No 1234/2008, <MAH> submitted to the Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary (CMDv) on <date> an application for a recommendation of an unforeseen variation.

The procedure started on <date>.

APPLICANT'S PROPOSAL FOR CLASSIFICATION

Applicant's proposal for the classification:

- | | |
|--|-----------------------------|
| <input type="checkbox"/> IA _{IN} (Immediate Notification) | <input type="checkbox"/> IA |
| <input type="checkbox"/> IB | <input type="checkbox"/> II |

Applicant's justification for the proposed classification:

RECOMMENDATION FOR CLASSIFICATION

Rapporteur's proposal for the classification:

IA_{IN} (Immediate Notification)
 IB

IA
 II

Justification for the proposed classification³:

CONCLUSION

The Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary (CMDv), having considered the application as set out in the justification, recommends the classification of the proposed unforeseen variation to the terms of the Marketing Authorisation as a type <IA_{IN}/IA/IB/II> variation.

[Delete one of the 2 options below as appropriate]

The <CMDh/European Medicines Agency> agrees with the above-mentioned recommendation of the CMDv.

The European Commission, CMDh and Rapporteur(s) have been informed consequently.

The <CMDh/European Medicines Agency> have divergent opinions on the classification proposed by the CMDv.

The European Commission has been informed consequently.

The following information will be published on the CMDv website:

Section of the Classification Guideline⁴	Date issued	Summary of the proposed change⁵	Proposed classification	Proposed conditions, where relevant⁶
<insert (e.g. B.I.a.1)>	<date>		<IA _{IN} /IA/IB/II>	
<insert (e.g. B.I.a.1)>	<date>		<IA _{IN} /IA/IB/II>	

³ In case an identical or similar variation application been published to other centrally/nationally approved products, please indicate reference

⁴ The recommendations should be grouped per section of the Classification Guideline to facilitate searching. Within each section the recommendations should be listed in a chronological order.

⁵ with commercially confidential information deducted in accordance with the principles laid out in the Guidance document on the Principles to be applied for the deletion of commercially confidential information for the disclosure of EMA documents (EMEA/45422/2006)

⁶ Conditions to be stated only for Type IA/IA_{IN} variations