Question and answer document concerning changes not covered by Variation Regulation 1234/2008 (as amended by Regulation 712/2012)

Version 2.8 (12 November 2024)

Contents

Introduction

The following changes are not covered by Variation Regulation 1234/2008 (as amended by Regulation 712/2012):

- Change of a marketing authorisation holder
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Change of a marketing authorisation holder

Change of a marketing authorisation holder (change of legal person/legal entity) falls outside the scope of Variation Regulation No. 1234/2008 (as amended by Regulation 712/2012). However, a **change of name** and/or a **change of address** of a marketing authorisation holder does fall within the scope of the Variation Regulation; in that case, the applicant must then state that the legal entity remains the same. This document explains how to submit a change of marketing authorisation holder (i.e. a change of legal entity).

In which cases is there a different legal entity?

The applicant must determine and declare that the legal entity remains the same and only changes its name, or that it concerns a different legal entity.

Who needs to submit the change of marketing authorisation holder?

The acting marketing authorisation holder must, in theory, submit the change to the MEB. It is also possible for the future marketing authorisation holder to submit the change to the MEB. In that case, the future marketing authorisation holder must submit a letter of authorisation, in which the acting marketing authorisation holder agrees to the new marketing authorisation holder submitting the change.

How must a change of marketing authorisation holder for an MRP/DCP product be submitted?

As the transfer of the marketing authorisation from one holder to another falls outside the scope of Variation Regulation 1234/2008 (as amended by Regulation 712/2012), the transfer of the marketing authorisation from one holder to another must be dealt with at national level. As a result, the same submission requirements apply to MRP/DCP products as to national products. The CMDh website states the following on this subject (www.hma.eu/20.html, Q&A on Variations, Question 2.8):

> ……
> However, the transfer of the MA to a new MAH is to be handled as an independent purely national application according to Art. 1(2) of the Regulation (EC) 1234/2008 as there is a change of the legal entity. The fees are set by each CMS and the management of the procedure is dealt with by each CMS. The current registered MAH should send a notification to the RMS to specify which CMSs and MAHs are concerned with this national procedure.
>
> Remark: The change in the name and/or address of the MAH (i.e. the MAH remains the same legal entity) for a product authorised through MRP or DCP, is processed at MRP level via a type IAIN No. A.1 variation.

What information must be submitted for a change of marketing authorisation holder for a national product (including MRP/DCP)?

1. An accompanying letter clearly stating that it concerns a change of marketing authorisation holder. This letter must contain the following informatio:
    a) Name, business address, telephone and e-mail address of the acting marketing authorisation holder
    b) Name, business address, telephone and e-mail address of the new marketing authorisation holder
    c) The products for which the marketing authorisation holder will change. If this is a long list of products, this information may be provided as an attachment.
    d) A declaration that nothing will be changed in the SmPC, package leaflet and labelling except the marketing authorisation holder and the product name, if applicable

2. A declaration from the acting marketing authorisation holder agreeing to the transfer

3. A declaration from the future marketing authorisation holder that it will take over all rights and obligations relating to the authorisation

4. Proof of establishment of the applicant in the European Economic Area

5. Modified SmPC (module 1.3.1.), both clean and track-changes versions

6. Modified package leaflet (module 1.3.2), both clean and track-changes versions

7. Modified labelling (module 1.3.3), both clean and track-changes versions

8. Mock-ups of the labelling

9. If educational materials regarding the product are applicable: modified documents (in which the name/address of the marketing authorisation holder has been changed, where necessary)

10. A summary of the Pharmacovigilance System must be submitted with the change of the marketing authorisation holder via the relevant variation notification in conformity with the Variation Guideline, also see Q&A 2.8 on the CMDh website (www.hma/eu/20.html, Q&A on Variations:

    "*In case of the transfer of a MA in one or more member state(s) the new summary of the pharmacovigilance system (human) or DDPS (veterinary) of the new MAH has to be submitted to all member states concerned via MRP variation (as type IAIN notification, C.I.8.a, or under category C.II.7 as applicable). This is also applicable when using the Art. 57 database (human only) as the classification guideline (C.I.8) also requires a "proof that the applicant has at his disposal a qualified person responsible for pharmacovigilance and a statement signed by the applicant to the effect that the applicant has the necessary means to fulfil the tasks and*

responsibilities listed in Title IX of Directive 2001/83/EC". Therefore, a variation for the introduction of a new summary of the pharmacovigilance system after a change of the MAH still has to be submitted, later changes of the contact details of the QPPV or location of the PSMF do not require variations anymore when they are introduced via the Art. 57 database.
A variation to submit the summary of the pharmacovigilance system will not be necessary in cases where the MA is transferred within companies belonging to the same parent company and the same PSMF will continue to be used."

11. Declaration that the new MAH does not have a marketing authorization for the "same medicinal product" via the central procedure (CP).

What should I do if the change of the marketing authorisation holder requires a change of the product name?

A change of marketing authorisation holder sometimes requires a change of product name. This is certainly the case if the product name includes a reference to the marketing authorisation holder (e.g. (an abbreviation of) the marketing authorisation holder's name). In that case, the product name must also be changed, as one specific reference may only be used by a specific marketing authorisation holder.

Where it concerns a change of marketing authorisation holder, the relevant marketing authorisation holders are requested to check immediately whether a change of product name is necessary or desirable. If so, the following applies.

For products authorised via a **national procedure**, both changes must be submitted together in a single application. Both changes will be processed as a single case. The documentation required for type IB variation no. A.2.b. must be submitted together with the abovementioned documentation. The documentation for the variation concerned (type IA/IB) must also be submitted for the DDPS or summary PSMF (see also point 10 under "What information must be submitted for a change of marketing authorisation holder for a national product (including MRP/DCP?)").

The modified SmPC, package leaflet and labelling (modules 1.3.1, 1.3.2 and/or 1.3.3) must list both the new marketing authorisation holder and the new product name.

For products authorised via the **mutual recognition procedure (MRP or DCP)**, the two changes cannot be submitted with a single letter, as the change of marketing authorisation holder must be handled at national level and the product name change must be handled at European level.

Likewise, the change of the summary of the DDPS must be submitted via a separate variation procedure via MRP in the RMS and all CMSs.

Marketing authorisation holders are asked to submit changes of marketing authorisation holders in parallel with the changes of product names, and to cross-reference the two accompanying letters.

When can I submit a change of marketing authorisation holder?

A change of marketing authorisation is preferably submitted where there is no currently active case for the relevant medicinal product pending (i.e. all variations previously submitted have been processed). However, sometimes this is not possible. Therefore, the MEB allows the possibility to submit a change of marketing authorisation holder while active cases for the relevant medicinal product are pending. However, the acting and future marketing authorisation holders should bear in mind that the contact person(s) in the pending cases will not change. After completion of the change of marketing authorisation holder, the MEB will keep sending any correspondence regarding the pending cases to the contact person(s) of the then previous marketing authorisation holder. For all cases started after completion of the change of marketing authorisation holder, the MEB will use the contact person as indicated in the application.

Which time lines apply?

A change of marketing authorisation holder is processed within 60 days. It is not possible to determine a guaranteed specific date for the change of marketing authorisation in advance.

Can a change of marketing authorisation holder be submitted for a replica marketing authorisation?

No, in principle it is not possible to change the marketing authorisation holder for replica marketing authorisations, as a contract has been drawn up between the marketing authorisation holder of the basic product (legal entity B) and the marketing authorisation holder of the replica product (legal entity A).
Only if the previous marketing authorisation holder of the replica product (legal entity A1) and the new one (legal entity A2) have merged or belong to the same group of companies may a transfer of marketing authorisation holder take place. In this transfer from legal entity A1 to legal entity A2 (under the condition described above), legal entity B must also agree to the changed relationship. After all, A1 and A2 may belong to the same group of companies, but they are different legal entities.

Can a change of marketing authorisation holder be submitted for a parallel import product?

Yes, parallel import products may be transferred to another marketing authorisation holder that has a permit for parallel import. The documentation that must be submitted is the same as listed under points 1, 2 and 3 for changes of marketing authorisation holders for national products (accompanying letter and declarations), as well as the following:

- Proof that the new marketing authorisation holder can act as a holder of a parallel wholesaler authorisation: the manufacturer authorisation and wholesaler authorisation (or the parallel wholesaler authorisation) of the new marketing authorisation holder
- Modified package leaflet (module 1.3.2), with a declaration in the leaflet that it concerns a parallel import product
- Modified labelling (module 1.3.3), both clean and track-changes versions.

Can I submit other changes together with a change of marketing authorisation holder?

Other changes cannot be submitted together with an application for a change of marketing authorisation holder, with the exception of a change of product name (if this is related to the change of marketing authorisation holder).

Do I need to consult the MEB in advance?

A change of marketing authorisation holder may apply to a large number of products, for example in the event of a merger or takeover. Moreover, certain developments may cause changes to, for example, the name of any authorised manufacturer of the products in question. In such cases, it is strongly recommended that you contact the Regulatory Information Centre (RIC) department in a timely manner in order to ensure processing occurs efficiently, both for the marketing authorisation holder and the MEB.

Article 61(3) procedure

What is an article 61(3) procedure and how must it be initiated?

Article 61(3) of Directive 2001/83/EC contains a procedure for changes to package leaflets, labelling and logos that are neither associated with changes to the SmPC (module 1.3.1) nor associated with changes to a variation procedure.

- Changes to the SmPC, package leaflet and/or labelling (module 1.3.1, 1.3.2 and/or 1.3.3) arising from a type I or type II variation are part of the type I or type II variation. For type IA and IB variations, only changes to the SmPC, package leaflet and labelling (module 1.3.1, 1.3.2 and/or 1.3.3) arising from the variation are accepted. **Any** other change must be submitted separately.
- Changes that **exclusively** concern package leaflets and labelling do not fall not within the scope of the Variation Regulation. The procedure for these changes is described in article 61(3) of Directive 2001/83/EC. Each proposal for changes to package leaflets and labelling must be submitted separately. Both clean and track-changes versions of the package leaflet must be submitted, along with a signed declaration that no changes other than those specified have been made.
  Where a proposal for changes to a labelling is submitted, a mock-up must be enclosed.

The MEB strives to process such applications within 90 days. However, you may not assume tacit approval on the part of the MEB if you have not received any reply confirming approval within this 90-day period.

The CMDh has published a number of documents regarding the article 61(3) procedure for MRP products (see http://www.hma.eu/101.html).
Where it only concerns a change of the Dutch version of the package leaflet and/or labelling for an MRP/DCP product (therefore not a change of the harmonised English version of these texts), the article 61(3) notification can only be submitted in the Netherlands.

For products that only have a national marketing authorisation, it is possible to initiate an article 61(3) procedure for several products if the change to all products is identical. In that case, a separate notification form (see CMDh website http://www.hma.eu/101.html) must be submitted for each product.
Moreover, an eCTD must be submitted for each product.

How should a change to the package leaflet or a replica marketing authorisation be submitted?

A change to the package leaflet of a replica authorisation (also referred to as ‘similar authorisations’) must be submitted if the package leaflet text of the basic product (i.e. the product on which the replica authorisation is based) has changed. Such a change must be submitted as an article 61(3) notification.

Switching legal status

Which variation application has to be submitted for a switch in the legal status of supply from Prescription only(PO) to Pharmacy only (PH) or Pharmacy and Drugstore only (PDO) and what documentation has to be submitted?

No variation procedure has been defined in the classification guideline for a national change of the legal status of supply (only for centrally authorised products).
A switch from prescription-only to pharmacy-only or pharmacy and drugstore-only status concerns a type II variation (product type 404). Category C.I.z may be used.
The following information/documentation should be submitted:

- A clinical overview.
- Justification/relevant data that supports the change of legal status. In that context, the MEB would also like to refer to the "Guideline on changing the Classification for the supply of a Medicinal product for human use" (see the website of the European Commission, Notice to Applicants Chapter 2C).
- If the switch in legal status of supply also implies that an increase in use is envisaged, an ERA (Environmental Risk Assessment) should be submitted.
  o Note: if no ERA is submitted, justification is required as to why this is not deemed necessary.
- Amended product information texts (SmPC/PIL, labelling and mock-ups) plus a user test should also be submitted.
    - Note: for MRP/DCP products, it is not possible to change the SmPC/package leaflet text during the procedure for switching the legal status of supply. In such cases, the indication must first be changed (if necessary) before the switch in legal status can be requested. In such cases the MAH is advised to contact the case manager for the procedure in question beforehand (so before submission of the variation).

Which variation application has to be submitted for a switch in the legal status of supply to General Sales (GS) and what documentation has to be submitted?

Please refer to the relevant information on the MEB website under GS legal status of supply.

No variation procedure has been defined in the classification guideline for a national change of the legal status of supply to GS (only for centrally authorised products). This request can be submitted using the subject line "Request for GS status". Depending on whether the active ingredient is already present on the list with GS status, the following variation applications may be applicable:

1) A type II variation application in category C.I.z for a change of the legal status of supply to GS for a medicinal product with an active ingredient that is not present on the GS list (product type 310). A type II variation is also required if the active ingredient is on the GS list but the conditions associated with that active ingredient on the list are not met.
2) A type IB variation application in category C.I.z for a change of the legal status of supply to GS for a medicinal product for which the active ingredient is present on the GS list and the associated conditions are met (product type 311).

Required documentation:
ad 1)

- the underlying scientific information and data including a justification as to why the medicinal product can be eligible for GS legal status of supply
- a declaration as to whether the OTC medicinal product complies with the 6 legal criteria that a medicinal product with GS status must meet
- amended product information
  Note: for MRP/DCP products, it is not possible to change the SmPC/package leaflet text during the procedure for switching the legal status of supply. In such cases, the indication must first be changed (if necessary) before the switch of legal status can be requested. In such cases the MAH is advised to contact the case manager for the procedure in question beforehand (so before submission of the variation).

ad 2)

- a reference to the published GS list on the MEB website plus justification as to why the medicinal product for which GS status is being requested matches the active ingredient on that list and complies with the conditions specified on the list.