

Q/A-LIST FOR THE SUBMISSION OF VARIATIONS ACCORDING TO COMMISSION REGULATION (EC) 1234/2008
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1. General questions

Question 1.1

What is the definition of MAH?

Answer:

According to the Commission Communication 98/C229/03 the definition of the same MAH is as follows:

Applicants belonging to the same mother company or group of companies and applicants having concluded agreements or exercising concerted practices concerning the placing on the market of the relevant medicinal product have to be taken as the same marketing authorisation holder.

Generally, in case of worksharing and grouping of IA variations for several MRP/DCP procedures the applicant should provide an explanation on the link between the MAHs.

Question 1.2

When will the Regulation (EC) 1234/2008 apply for purely national authorisations?

Answer:

Regulation (EC) 1234/2008 shall only be applicable for “purely national” procedures once the Regulation is updated to include variations to “purely national” marketing authorisations and this update has come into effect. After that moment in time, certain products under specific conditions may still be excluded based on a general decision of a Member State (See Article (2) of Directive 2009/53/EC).

Independent of Commission legislation, Member States may decide to implement similar procedures and classification of variations under national legislation for their variations to “purely national” marketing authorisations from January 2010 on.

Question 1.3

Is a fee foreseen by the CMD(h) for an article 5 request for a recommendation on an unforeseen variation?

Answer:

No.

2. Questions relating to the submission of variations

Question 2.1

When and how should the variation be submitted to RMS and CMS?

Answer:

According to the Regulation (EC) 1234/2008 the same application and the same documentation shall be submitted simultaneously to the RMS and all CMS.

Question 2.2

Is it necessary to submit variation applications to all concerned member states even if they are not concerned by the specific change (e.g. change in the address of the MAH in only one CMS)?

Answer:

Yes, the applications have to be submitted to all concerned member states.

Question 2.3

Which documents have to be submitted for a variation Type IA, IB or II or a grouped application before a procedure is started?

Answer:

The application form incl. all relevant documentation (e.g. SmPCs, labels and leaflets as required, national product information texts (not applicable for Type II), relevant pages from the Guideline with ticked boxes for conditions and documentation for Type IA and/or Type IB etc.) has to be submitted to the RMS and all CMS. The procedures will not be started before the RMS has received the dispatch list with the dispatch date for all CMS including a statement of the applicant that the fees have been paid, where applicable.

Question 2.4

Currently, no variations should be submitted during ongoing Repeat Use Procedures (RUP). What about the annual reports or Type IA variations with immediate notification? Do they have to be submitted before starting a RUP though the 12 months are not full in order to have the dossiers complete?

Answer:

Applicants should carefully plan a strategy for their procedures. Annual reports may be submitted earlier than the 12 month deadline in order to have the dossier adequately updated before starting a RUP procedure. Type IA variations with immediate notification have to be submitted before the start of a RUP.

Question 2.5

Currently, no variations should be submitted during ongoing renewal procedures. What about the annual reports or Type IA variations with immediate notification? Do they have to be submitted before starting renewal though the 12 months are not full in order to have the dossiers complete?

Answer:

Applicants should carefully plan a strategy for their procedures. Annual reports may be submitted earlier than the 12 month deadline in order to have the dossier adequately updated before starting a renewal procedure. Type IA variations with immediate notification may in exceptional and urgent cases be submitted during a running renewal procedure. The RMS has to be contacted in advance.

Question 2.6

When do I have to submit national translations for a variation procedure?

Answer:

For Type IA and Type IB variations the national translation(s) have to be submitted together with the application. For Type II variations national translation(s) have to be submitted within 5 days after the end of the procedure.

3. Questions relating to the Classification of a variation

Question 3.1

Which Type of variation should be submitted when the particular change we are applying for is not mentioned in the classification guideline or one or more of the conditions cannot be fulfilled?

Answer:

If a change is not mentioned in the Annex II of the Variation Regulation (EC) 1234/2008 or the classification guideline or the conditions for a specific change could not be fulfilled and the change is not already classified as a Type II variation, this change can be submitted as a Type IB variation by default. However, if the change in the view of the applicant has a significant impact on quality, safety and efficacy of the product, a Type II variation has to be submitted.

Question 3.2

How to apply for the deletion of more than one manufacturing site?

Answer:

In case more than one manufacturer in one MA has to be deleted one single Type IA notification (grouped application) for all manufacturing sites has to be submitted. However, it has to be assured that there is still one approved manufacturing site left in the documentation.

Question 3.3

Which procedure type is applicable for the implementation of the Core Safety Profile into the SmPC and the PL after a PSUR worksharing procedure?

Answer:

The implementation of change(s) requested by a National Competent Authority following the assessment of a Periodic Safety Update Report is listed in section C.I.3 of the Classification Guideline. The implementation of a Core Safety Profile can be submitted as a type IB variation provided no new additional data are submitted by the MAH. The revised PL (which is not agreed upon in the PSUR worksharing procedure) is not considered to be 'new additional data'. However, if the implementation of the Core Safety Profile needs to be substantiated by new additional data submitted by the MAH then a type II variation must be submitted.

4. Questions relating to grouping and worksharing

Question 4.1

Can the same variation for more than one marketing authorisation be submitted on one application form?

Answer:

Yes, in case of worksharing applications and type IA notifications for several MRP/DCP marketing authorisations one single application form is to be submitted for all marketing authorisations of the same holder concerned. However, for Type IA notifications it is highly recommended to combine only marketing authorisations of the same RMS.

Question 4.2

If there are different Marketing Authorisations holders for the same MRP product in the CMS, may these products participate in grouping and worksharing?

Answer:

Generally, all MAHs belonging to the same MRP or DCP are regarded as the same MAH and the procedure may participate in grouping and worksharing.

Question 4.3

Is it possible to submit one grouped application for different marketing authorisations?

Answer:

A marketing authorisation in the sense of variations is defined as one MRP or DCP product including all strengths and forms. Several marketing authorisations of the same MAH can be grouped together in the case of Type IA notifications (also applicable as "annual report") if the changes applied for are identical. A grouping of more MAs is not possible for Type IB and Type II variations. The CMS in all the concerned marketing authorisations may differ. Please see also detailed information in chapter 6 of the Best Practice Guide.

Question 4.4

When has an 'annual report' to be submitted?

Answer:

The so-called "annual report" is no specific procedure but a submission of single or grouped Type IA variations within a maximum of 12 months after the implementation of the first Type IA change which is part of this submission. It is up to the applicant if and when to submit an annual report. The submission of Type IA notifications in the form of an annual report is not mandatory. The annual report for Type IA notifications not requiring an immediate notification has to be submitted at the latest 12 months after implementation of the first Type IA variation.

Question 4.5

Can harmonisation of Module 3 be done by worksharing?

Answer:

Module 3 harmonisation is surely an option for worksharing as worksharing does not require product harmonisation **in** advance. The aim is to have a harmonised result. However, currently the procedure may only be used for MRP/DCP licences as the Regulation (EC) 1234/2008 is not yet applicable for purely national licences (see also question 1.2).

Question 4.6

Is it possible to group Type IA variations for a CP and a DCP product if the Rapporteur and RMS are from the same Competent Authority?

Answer:

No, CP and MRP/DCP products may only be combined in a worksharing procedure, not in any other type of procedure.

Question 4.7

Is the reference authority for a worksharing procedure automatically the RMS of one the products concerned?

Answer:

The reference authority for a worksharing application is chosen by the CMDh, based on a proposal by the applicant. However, the reference authority has to be a MS concerned in at least one of the procedures.

5. Questions regarding the approval and implementation of variations

Question 5.1

Is there a possibility for an appeal by the MAH in case of rejection of type IB or type II variations?

Answer:

According to the Regulation (EC) 1234/2008 a referral to the CMD is only possible in case of potential serious risk to public health seen by a CMS. Therefore, there is no possibility for the applicant in case of an MRP or DCP procedure for any type of variation to refer the matter to the CMD or the CHMP.

Question 5.2

What is meant by “implementation” for Type IA variations?

Answer:

For quality changes, implementation is when the Company makes the change in its own Quality System.

This interpretation allows companies to manufacture conformance batches and generate any needed stability studies to support a Type IAIN variation before making an immediate notification¹ because the change will not be made in their own Quality System until these data are available.

For changes to the pharmacovigilance system (DDPS), ‘implementation’ is when the Company makes the change in its DDPS (i.e. when it internally approves the DDPS incorporating the changes).

For product information, it is when the Company internally approves the revised product information. The revised product information will then be used in the next packaging run.

Question 5.3

If a Type IA variation is part of a group containing Type II, do I have to wait for the implementation of the IA variation until the group assessment is completed?

Answer:

The principle of Type IA notification applies also when the Type IA variation is part of a grouped application. The Type IA change is implemented before submission of the grouping. Only in case a Type IA change is dependent on the outcome of other changes in a grouped application this change may be implemented as soon as the complete grouped application is approved.

¹ For example the type IAIN for addition, deletion or replacement of components in the flavouring or colouring system requires stability data on at least two pilot scale or industrial scale batches.

Question 5.4

In case SmPC changes are applied for in a Type II variation when can I implement the national texts?

Answer: 30 days after submission of high-quality national translation(s) of the product information the changes are implicitly approved. A MS has to comment on the national translation(s) within 29 days or otherwise the proposed translations are implemented.