Public consultation paper – Review of the Variations Regulation
Review of Commission Regulation (EC) No. 1234/2008

Comments of the CMDh

General remark:
We would like to clarify with the EC that homeopathic and herbal medicinal products subject to a registration procedure are still not concerned by the provisions of the revised Variations Regulation.

The rules for the variation of purely National authorisations should wherever possible be identical to those for variation of DC/MR or Commission authorisations and this particular change should be implemented as soon as possible.

Consultation item no. 1:

Do you agree that where dossiers are not harmonised difficulties could raise for worksharing when accepting the assessment carried out by one member state by other member states?

No, the worksharing procedure is already practised successfully for MRP/DCP products that are not harmonised in advance. It may be extended for purely national products in the same way without any problems to be expected. This procedure is regarded as one of the main advantages of the extension of the Variation Regulation to purely nationally licensed products for the applicants as well as for the NCAs.

The use of worksharing procedures especially for nationally authorised products will encourage the submission and the adoption of harmonised wordings for concerned medicinal products in EU without the need to have a priori harmonisation of the dossier. However, the companies should check before the submission of the worksharing applications that the proposed changes are not in contradiction or inconsistent with the information already included in the marketing authorisations.

There is a corresponding information given in the procedural guideline and we would propose to include this information in the revised Variations Regulation:

In order to benefit from a worksharing procedure, it is expected that the same change(s) will apply to the different medicinal products concerned, with either no or limited need for assessment of a potential product-specific impact. Therefore, where the ‘same’ change(s) to different marketing authorisations require the submission of individual supportive data sets for each medicinal product concerned and separate product-specific assessment, such changes will not benefit from worksharing.

General comment on the worksharing procedure: MS and Industry have concerns regarding the complexity of the procedure to appoint reference authorities for worksharing. At present the CMDh has to appoint a reference authority for all worksharing, even if all procedures have the same RMS. It should be considered if the CMDh always needs to be involved and how the procedure could be simplified (moreover, it should be noted that the current Regulation foresees the appointment of a reference authority AFTER a worksharing variation is submitted which is not feasible).

Consultation item no. 2:

Which option a) or b) mentioned above do you consider that should be adopted to allow worksharing ?

Neither a) nor b) are supported. There is no need to include any restrictions for worksharing procedures for purely national products in the Regulation. The procedure without harmonisation in advance is already common practice for MRP/DCP products and no problems have occurred.

See also the answer given to consultation item no. 1.

Consultation item no. 3:

Do you agree with the principle that the deadline for adoption of Commission Decisions amending marketing authorisations must be driven by public health considerations?

The problems described are restricted to centrally authorised products. Generally it is agreed that the deadline for adoption of Commission Decisions must be driven by public health considerations but these deadlines may not be longer than the current timelines. A definition for such changes with impact on public health has not been given so far and is probably difficult to determine, e.g. warnings etc.

However, before coming to a conclusion on this topic we would need more clarification on how these definitions should look like.

Consultation item no. 4:

Which category of variations do you consider that should be adopted within shorter deadlines?

All changes having an impact on the benefit/risk profile of the medicinal product, e.g. all changes to classification guideline categories C.I.1-C.I.3 should be adopted within short timelines as these categories of type IB have been introduced in order to make the rapid implementation of safety-relevant changes possible. Furthermore, there might be some urgent changes to Module 3 (with acceptable justification) necessary to be adopted with shorter timelines.

Generally, applicants should be advised to make more use of other procedures like grouping and worksharing in order to reduce the number of single changes on the product information.

Consultation item no. 5:

Do you agree to extent the current system that allows holders to implement certain variations prior to the adoption of the Commission Decision (to the exclusion of those changes with most impact for public health)?

If it is in agreement with the legal framework of the Union to implement changes in centrally authorised products before the adoption of the Commission Decision the extension of the current system would be highly appreciated. Changes having an impact on the benefit/risk profile of the medicinal product should then be implemented after the Opinion.

Consultation item no. 6:

Do you consider appropriate to introduce a deadline for the implementation of changes to product information significant from a public health standpoint?

No, CMDh does not see the need to introduce a deadline for the implementation of changes to product information significant from a public health standpoint.

According to Article 24 (5) of the Commission Regulation (EC) 1234/2008 the implementation dates for changes having an impact on the benefit/risk-profile of the medicinal product are already considered:

"5. Urgent safety restrictions and variations which are related to safety issues shall be implemented within a time frame agreed by the holder and the relevant authority and, in the case of a centralised marketing authorisation, the Commission."

A new discussion is therefore not regarded necessary. However, as a general remark it should be stated that the system should be kept as simple as necessary and any further increase in complexity should be avoided. It should be assured that changes with an impact on the safety of the medicinal product are implemented immediately.

Consultation item no. 7:

Do you agree with the above analysis?

No, this seems to be a specific administrative problem for centrally authorised products. The NCAs are handling changes in the product information of MRP/DCP in a completely different way then the Commission does for CP.

We strongly support the need to reduce the number of variation procedures. A more flexible approach regarding acceptance of grouping of variations might be helpful, especially with regards to the updates of SmPC and PLs.

Consultation item no. 8:

Do you consider appropriate to extend the time limits for assessment of complex grouped applications to enable a larger amount of cases where grouping under one single application could be agreed by the competent authority?

Yes, we would be in favour of extending the time limits for complex variations and to allow them to be submitted as single change applications. However, this would require a strict definition of complex variations in the legislation and/or the classification guideline, comparable to Annex V of the Regulation. We propose to introduce such changes as single type II complex variations in order to reduce the administrative burden for NCAs and the pharmaceutical industry. However, it should be made clear that:

- the submission time point is agreed with the relevant competent authority before submission
- a proposal for time limit for complex variations of 90 days (as for procedures in Annex V) is included and that
- a detailed description of the proposed changes (e.g. in the application form present/proposed) is provided. If this is lacking the variation application will be invalidated.

Consultation item no. 9:

Do you think that changes to the procedure in Article 21 of the Variations Regulation are necessary?

A high degree of flexibility is necessary with regard to the amount of data needed at submission and at authorisation depending upon the lead time between identification of a pandemic and its impact on the Community. Changes to the overall guidance for influenza vaccines are currently under consideration. Therefore changes to Art. 21 are currently not proposed. However, it should be clarified whether the classification system by WHO on the pandemic situation really is the most appropriate system.