MINISTERIO DE SANIDAD Y CONSUMO
agencia española de medicamentos y productos sanitarios

DIRECCIÓN DE LA
AGENCIA ESPAÑOLA
DE MEDICAMENTOS Y
PRODUCTOS SANITARIOS

UAP/INTE/LFG

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Madrid, 15 February 2008

Re: Revision of the Variations Regulations: public consultation of the "comitology" part

Dear Mr. Rossignol,

Please find enclosed the comments on the Public Consultation on the "comitology" part of the revision of the Variations Regulations. I kindly ask you to consider them and I apologize for the delay sending the comments and for any inconvenience.

Yours sincerely,

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SPANISH COMMENTS ON VARIATIONS REGULATION REVIEW
Version 24 October 2007

The Spanish Agency of Medicines and Medical Devices totally supports to the European Commission in the intention to make the regulatory framework on changes to medicinal products (the "Variations Regulations) simpler, clearer and more flexible.

After revision of the draft Commission regulation concerning the examination of amendments to the terms of marketing authorizations for medicinal products for human and veterinary medicinal products (version 24 October 2007), please find below the following comments:

Article 4. Classification of variations. "Type IB by default"

- We prefer keep the classification by default of variations of Type II. But we are not against to consider them as Type IB variations as it is established in this modified regulation provided that this clarification is included: "It is optional to the Competent Authorities to switch to a type II variation".

- This change can be a problem for veterinary immunological products, so it will be necessary to revise all the guideline.

Article 5. Scientific recommendation on unforeseen variations

- The scientific recommendation does not have legal binding for the National Competent Authorities. This can lead to conflicts related to the misinterpretation or misunderstanding of the classification of the variations. It is doubtful to simplify the procedure with this change.

Article 7. Grouping of variations

- It will be important to include that all the changes that happens in a grouping of variations have to be well defined and specified in the single notification which covers all the variations, and not only in the scientific documents.

-Where several type IA variations of several marketing authorisations are grouped and there is just only a single notification that covers all such variations, this increase the administrative burden of the National Agencies . This can not be supported. We consider that the grouping of variations for each marketing authorization can be useful, but not for several marketing authorisations owned by the same holder, or mixing different authorization procedures (pure national, RM, decentralised and centralised procedures).

Article 8. "Do and Tell" procedure for Type IA variations.

- It would be important to define and explain in the Regulation the notification procedure and to specify the differences between this procedure and the others (i.e if we have to validate the documents, and if it's necessary to approve or. reject it).

- We also see problems to reject some modifications that have been implemented in the past.

- If we receive an annual report compiling all "do and tell" changes made in the last twelve months in a certain product, and if we receive a lot of modifications, one month to close the procedure maybe will not be enough to revise all of them. In fact type IA variations are the most common and numerous (we should do the annual work of each product within only one month).

- Also the grouping of variations will make it more complicated, and we also express concern about the workload that this procedure would entail on the National Agencies.

- Another problem arises if we receive a type IB or II variation which includes a change corresponding to a type IA variation already implemented, but it has not been still notified, because the applicant will send all this variations as an annual report.

- It can be necessary to review all the guideline (the classification and conditions of all variations), because some type IB, IA and "IA in" variations could make some problems in opinion of our evaluation team.

- In case of the "Do and tell" procedure is finally accepted, the scope of this procedure should be clearly defined.

Article 24. Worksharing procedure

-The authority that have studied the dossier and issued the marketing authorisation is a Member State in the case of pure national authorisations, or the RMS in community procedures. These states are the ones which have all the information about the product and their changes and the consequences in the human and animal health in their countries. So in our opinion, it will be a problem to downscaling the classification of the change because this implies that there will be scientific consequences. In fact if we have a type IB that turn into IA the procedure will be a notification with no evaluation of the change, and if it's a type II or an extension that turn into a type IB we will have less time to evaluate the change and give a final opinion (when these kind of changes are usually very important). In fact with the new regulation if we do not give an opinion within 30 days the change shall be deemed accepted (art. 9).

- There is still more concern with downscaling in case A (page 8, point 6 consultation paper) where the change concerns one given medicinal product that is authorised at purely national level in several Member States, because it doesn't matter if it is a type II, IB or an extension, the downscaling leads always to a type IA with no evaluation, because is a notification procedure.

- On the other hand this downscaling procedure is not defined in the Regulation text and it is only described in the consultation paper.

- The final responsibility of the authorisations of the changes relays on the value of a previous opinion of the EMEA and this is unclear attending to the legal definition and functions of this European Organization in the current Regulations. It is anomalous that the EMEA may issue an opinion on variations or extensions of medicinal products authorised by national procedures, when the whole documentation is located in the National Agencies. Therefore the EMEA would issue an opinion based only in the documentation included in the application.

- We consider unjustified that the EMEA take part in the evaluation of variations and extensions of national medicinal products. Due to the CMDs have extensive experience of processing variations for products authorised nationally and through mutual recognition /decentralised procedures, this group would be a more appropriate committee to deal with these variations.

Others general comments

- Referring to Type II definition it would be better to say: a variation which is not an extension, and which has substantial changes on the quality, safety or efficacy of the medicinal product concerned, instead of: a variation which is not an extension, and which has substantial potential to have a negative impact on the quality, safety or efficacy of the medicinal product concerned.

- Due to the fact that the extensions of a marketing authorization are considered as a new register or a new marketing authorisation (except in some cases like additional species for veterinary products), they are out of the scope this regulation. But in the Regulation the extension of a marketing authorisation definition only gives the possibility to be a variation Therefore, extensions should be excluded of this regulation or we would like to treat both ways as a change that shall granted authorisation or as a change to be included in the initial marketing authorisation.