PPTA
Plasma Protein Therapeutics Association

5 October 2011 **BY E-MAIL**
Reference: DGSanco11005

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Subject: Variations Regulation: Plasma Master File 2nd step

Dear Madam, Sirs,

In 2010, PPTA and other associations representing manufacturers of biological products have written to you to inform you about significant flaws of the new variations regulation (DG Sanco 10001, 25 May 2010; DG Sanco 10002, 29 June 2011). While some of these issues have been resolved, which is greatly appreciated, there are still unnecessary regulatory hurdles which cause a significant administrative burden on regulatory authorities and manufacturers.

We have noted that the 2011 workplan of the CMDh also contains a mandate to continue to contribute to further improvement of the handling of the Variation Regulation and Worksharing procedures foreseen after implementation of the Directive for national procedures. It is very important that the Directive will be implemented for national procedures, because currently, there is no worksharing for CP/ MRP / DCP including national licenses.

The implementation on national level is certainly a matter of priority, but we would respectfully like to point out that there are other remaining issues that would need the attention of the CMDh and other European and National regulatory bodies. In the Public Consultation Paper on the Review of Commission Regulation (EC) No 1234/2008) stakeholders are consulted on the adjustment of some of the procedures with a view to focus resources of the authorities on variations with the most impact on public health. The PMF 2nd step procedure, a purely administrative act after a centralized evaluation of the PMF, certainly has no impact on public health and unnecessarily binds resources of national

regulatory authorities, which could be more efficiently used in areas of real impact on public health.

In our previous submission in May 2010 we have presented a case study describing the 2nd step procedures before and after the implementation of EC/1234/2008. We demonstrated that the workload for the company and also the involved regulatory authorities significantly increased because for this step "of purely administrative nature" (Guideline on PMF and VAMF "Second Step") now each single product dossier has to be updated resulting in an increase of electronic sequences from 1 to 100. In addition, the associated costs have exploded to 740% in the case presented in 2010. Since then PPTA member companies have gathered more experience with the 2nd step procedure verifying that the first case reported in 2010 is still representative for all our member companies.

We believe that the current procedure is a waste of already limited resources on the side of the manufacturers as well as on the side of the National Competent Authorities (NCA). It is also not in line with the EC's better Regulation Initiative that aims to avoid unnecessarily complicated regulatory procedures.

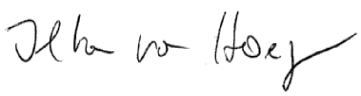
We would therefore respectfully like to propose to simplify the PMF 2nd step procedure..at least for the "*inclusion of an updated/amended PMF, if the properties of the medicinal products are not affected"*. For this case, we would consider a mere notification of the concerned competent authorities, without necessity to provide a product or PMF related sequence, as fully sufficient. Regarding the documentation we would propose to provide the product specific declaration of applicability and expert statement. However, documents that are already available for all competent authorities elsewhere (e.g. PMF certificate, evaluation report), should just be quoted by referencing, as is common practice e.g. for pharmacopoeia monographs. This referencing procedure should be possible for all changes to a PMF.

The proposed adaption would require minor efforts, namely marginal updating of two regulatory documents (2nd step guideline, Guidelines on the details of the various categories of variations Regulation (EC) No 1234/2008Article 4(1)(a)). A concrete proposal is reflected in the attached guideline excerpts, which would lead to a significant simplification for the industry as well as for the authorities without any loss of relevant information.

PPTA member companies are willing to pay a fee comparable to the fee for a type IA_{IN} variation for this simplified procedure to avoid any financial disincentives for the NCAs, despite the fact that the notification procedure prior to EC/1234/2008 was free of charge.

We hope that you will consider our proposal and remain at your disposal for further discussion.

Yours sincerely,



Dr. Ilka von Hoegen

Senior Director, Quality and Safety

Attachments:

- Proposed update for 2nd step guideline

- Proposed update for Guidelines on the details of the various categories of variations Regulation (EC) No 1234/2008Article 4(1)(a))